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The Use of the Systemic Hemostat Carbazochrome Salicylate

J. C. Bacala, M.D.

(Abstracted from the Western Journal of Surgery, Obstetrics, and Gynecology, 64:88 (1956)

The author emphasizes the need for dependable chemical control of bleeding and oozing, and reviews the methods that have been tried to attain hemostasis, including the use of vitamin K and bioflavonoids.

He gives the history of carbazochrome salicylate and describes the clinical work completed to demonstrate its effectiveness. It appears to be specific for conditions characterized by increased capillary permeability. It has no effect on large blood vessels; it does not alter blood components; it does not affect blood pressure or cardiac rate. It has neither vasoconstrictor or vasodilator action. The drug has no known contraindications.

He reviews 1051 cases from the files of St. Anthony Hospital, Louisville, Kentucky, of which 330 were treated with Adrenosem Salicylate. 317 were surgical cases and 13 obstetric-gynecological conditions. The treatment was given for symptomatic relief, and as a clinical recourse for patient safety.

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The author points out that in pregnancy, seepage bleeding occurs more because of capillary permeability, and in spite of increased coagulability. Here, Adrenosem becomes specific for strengthening capillary resistance.

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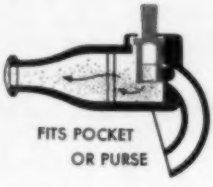

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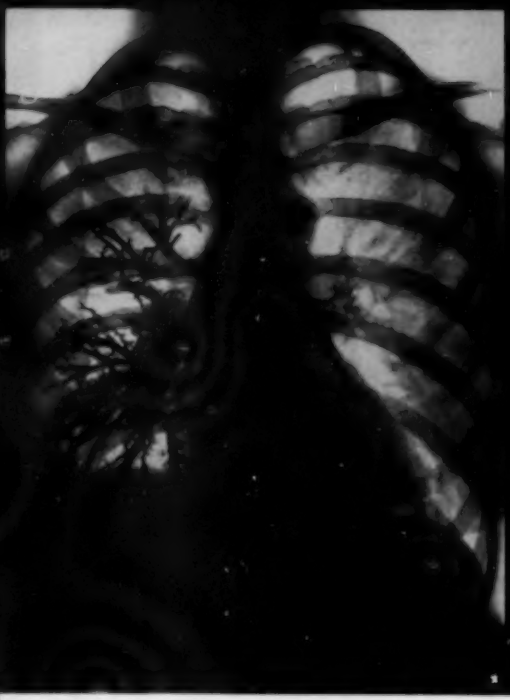

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1. Burrascano, J. J.: Sea View Hosp. Bull. *15*:149 (July) 1955.

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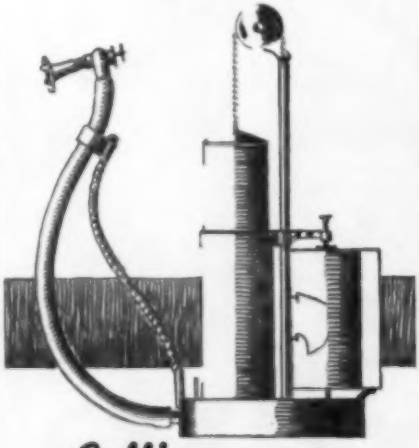

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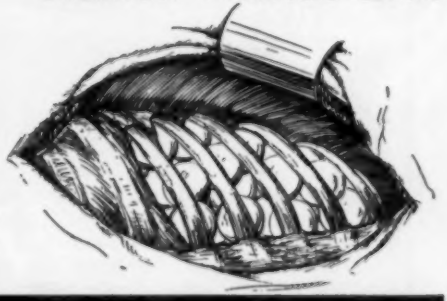

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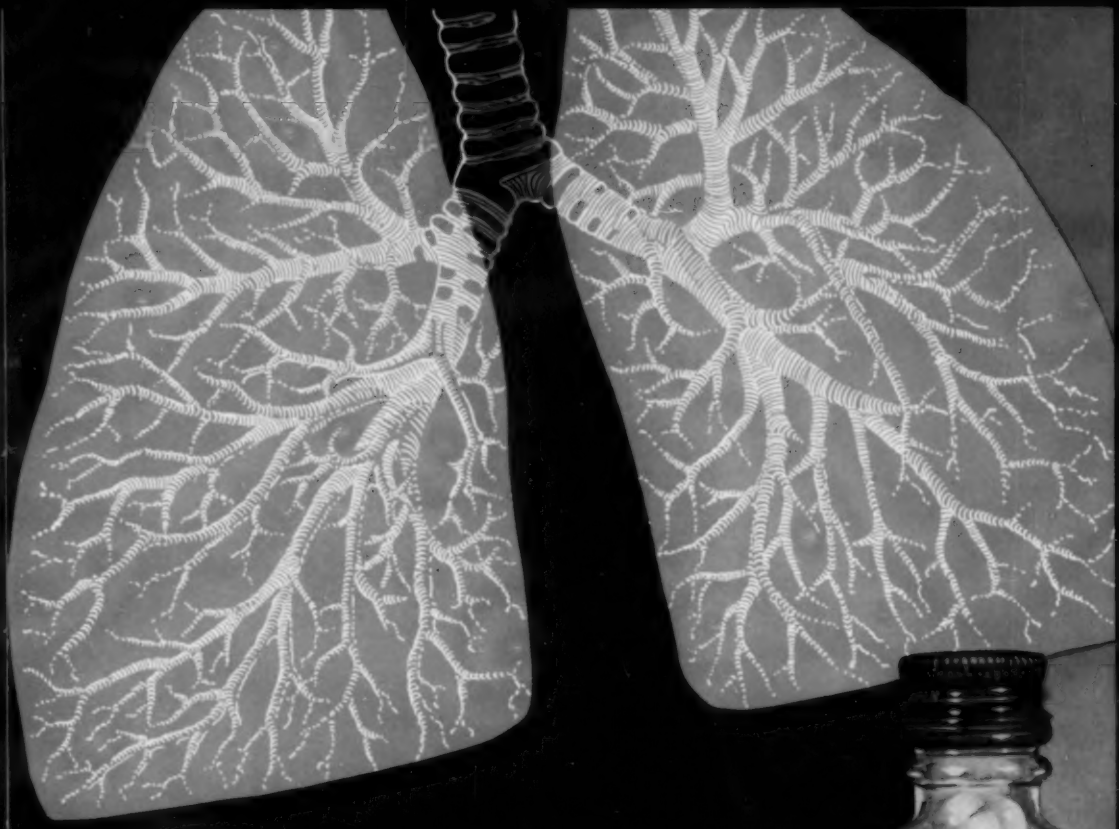

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References:
1. Winsor, T.: Am. J. M. Sc. *230*:133 (Aug.) 1955. 2. Grimson, K. S.: J.A.M.A. *158*:359 (June 4) 1955. 3. Grimson, K. S., Tarazi, A. K., and Fraser, J. W., Jr.: Circulation *11*:733 (May) 1955. 4. Grimson, K. S., Tarazi, A. K., and Fraser, J. W., Jr.: Angiology *6*:507 (Dec.) 1955. 5. Strawn, J. R., and Moyer, J. H.: Personal communication, 1955. 6. Maxwell, R. D. H., and Howie, T. J. C.: Brit. M. J. *2*:1189 (Nov. 12) 1955.

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6	75 mg.	75 mg.
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44	50 mg. daily	35 responded well; 14 of these became normotensive. All patients received reserpine as base therapy.	**	5
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The Post-Congress Tour to Wiesbaden, Heidelberg, Baden Baden, Munich and Vienna, will begin on Friday, August 24, and end in Vienna on August 30, where the Fifth International Congress on Bronchoesophagology will be held August 31-September 1 and 2.

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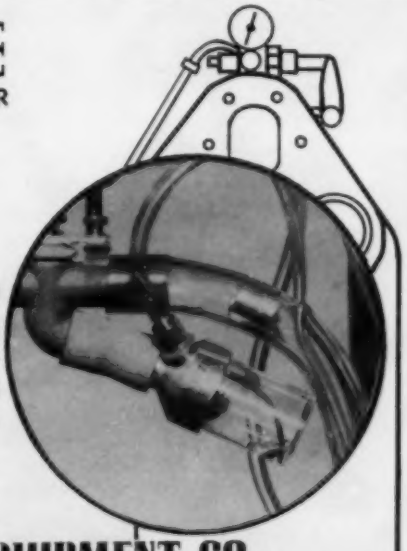

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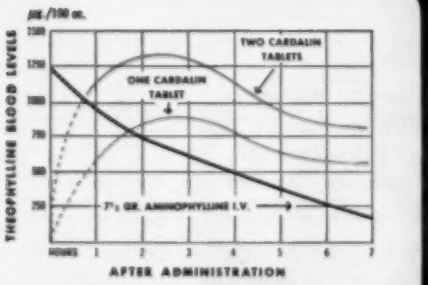

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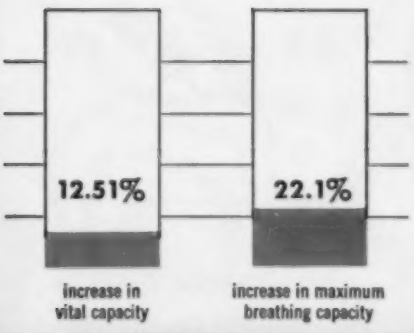

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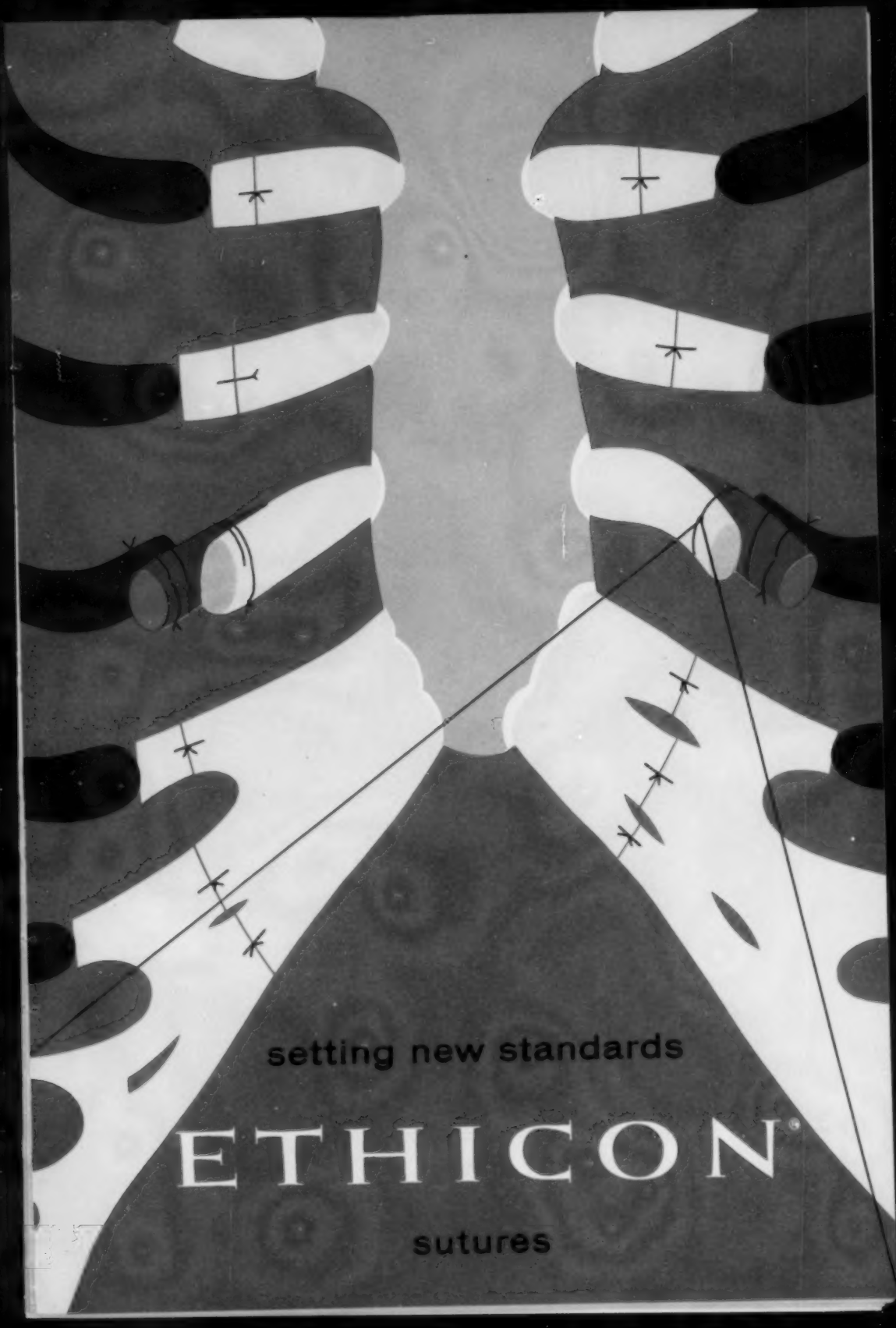
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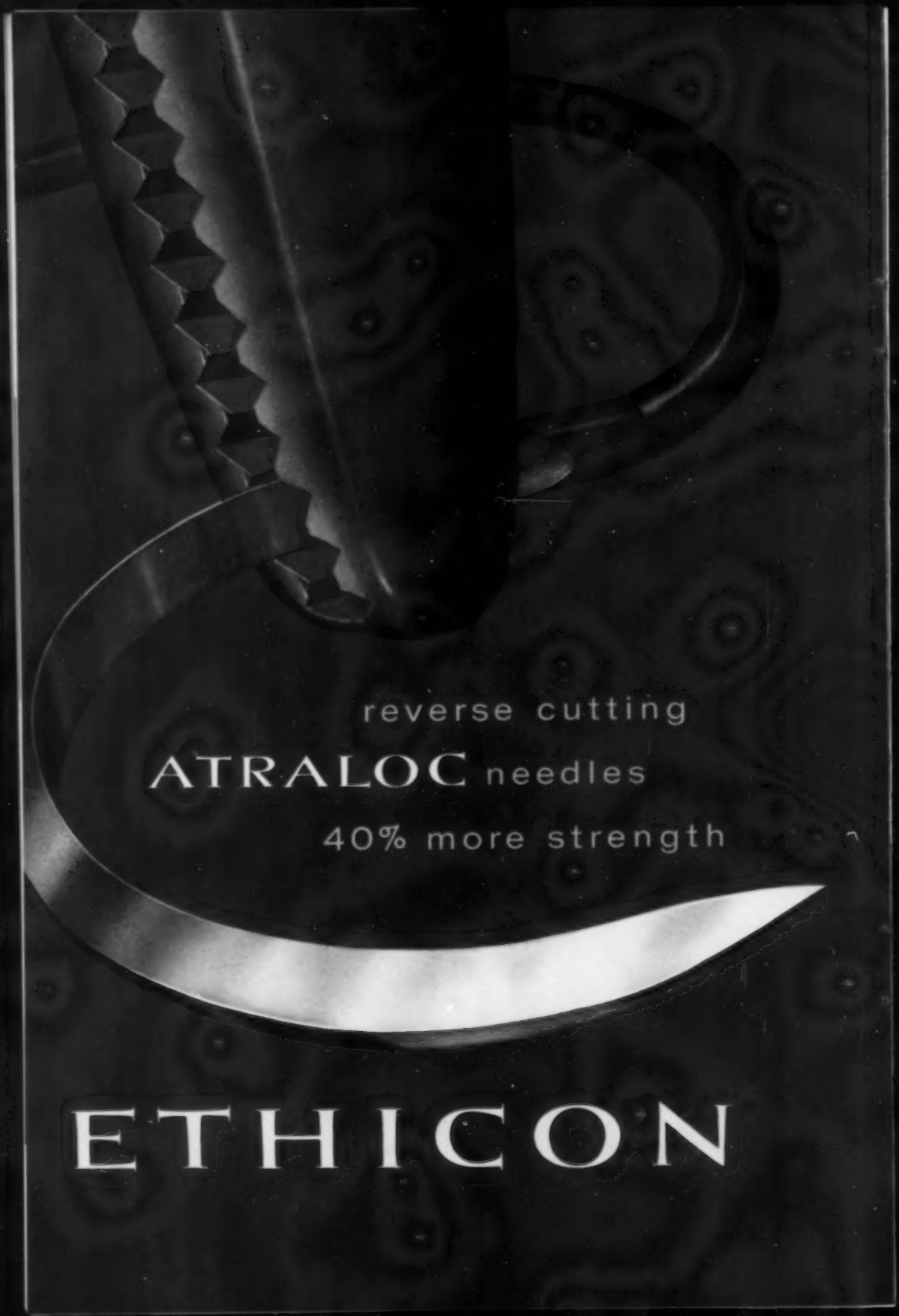
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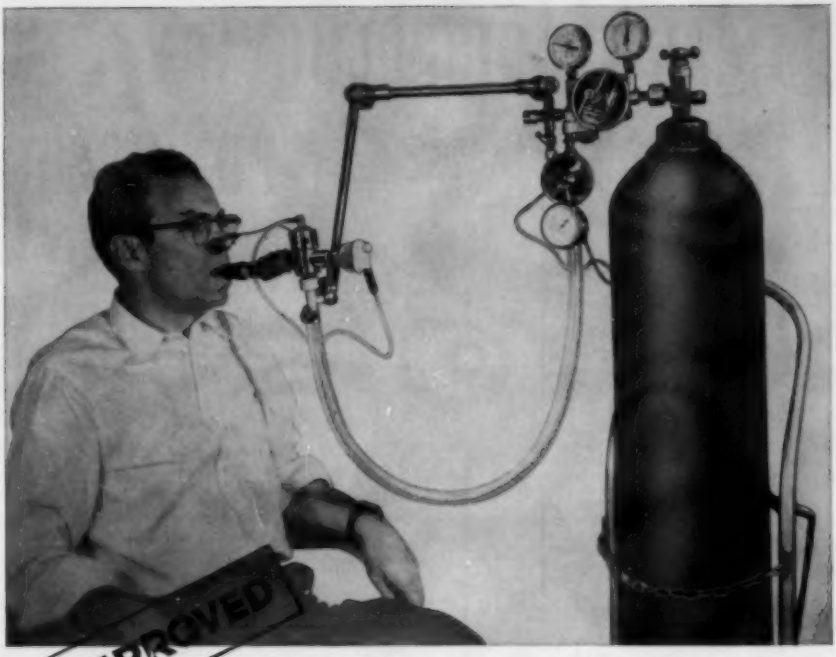

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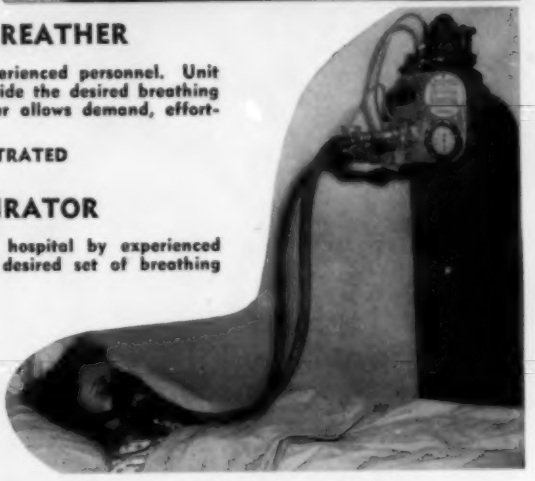

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VOLUME XXX JULY, 1956 NUMBER 1

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J. ARTHUR MYERS, M.D., F.C.C.P.

Minneapolis, Minnesota

The time has arrived when every physician, whether in general practice or a specialty, should actively engage in the tuberculosis eradication movement. In the history of man, the present moment offers the greatest hope for the ultimate eradication of this disease. It is no longer a problem of inability to diagnose early, to treat successfully in most instances, or to prevent its spread. These are reasonably well in hand. The current problem is the prevalence of tuberculosis. Even in so-called low incidence areas, more people have tuberculosis in some stage of its evolution than any other major disease.

The most serious disease scourge of mankind since the dawn of history, tuberculosis, wreaked destruction among animals and people until the present century. No effective weapon against it had been found. It long ran neck and neck with malaria as an incapacitator and killer. With the use of effective malaria control measures, tuberculosis is in bold relief as the cause of incapacity and death among the 2,400,000,000 people of the world. However, in a few places phenomenal accomplishments have been made in the last decades.

Mortality

When this century opened, almost 200 persons per 100,000 population in the United States were dying annually. However, the efficacy of education, sanatoriums, and control among animals soon became manifest. Mortality rates decreased, reaching 10.2 per 100,000 in 1954. In recent years, the age distribution of deaths is significant. The number of deaths among persons 25 years or younger decreased markedly. From 60 to 75 per cent of the deaths have been occurring among persons of 40 years or older, and approximately 40 per cent among those of 65 and older. These persons

*Presented before Tenth Postgraduate Course on Diseases of the Chest, Illinois Chapter, American College of Chest Physicians, Chicago, October 4, 1955; Ohio State University Postgraduate Course in Pulmonary Diseases, Columbus, October 7, 1955; Annual meeting, Minnesota Academy of General Practice, Minneapolis, October 19, 1955; Alameda-Contra Costa Medical Association, Oakland, California, January 16, 1956; Indianapolis Medical Society, Indianapolis, Indiana, April 10, 1956; Joint Session, North and South Dakota State Medical Associations, Aberdeen, South Dakota, June 5, 1956; and Council on Public Health, Committee on Indian Affairs and Committee on Liaison with State and County Medical Societies (American College of Chest Physicians), Chicago, June 7, 1956.

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belong to that generation which received almost no protection against tubercle bacilli as infants and children. They are like the generations which preceded them, when approximately 100 per cent became infected during childhood. For this generation (now the older people, 40 or above) the sanatoriums were built. They paid the price in loss of life, which caused mortality rates to soar. They paid the price in prolonged incapacity which filled sanatoriums and left large numbers to be cared for in homes. They paid the price by infecting their children and other associates, many of whom were doomed to illness and death. The surviving members of this older generation are now contributing a preponderance of the deaths from tuberculosis annually. Apparently these older people are breaking down and dying from tuberculosis they contracted in childhood. They have ever since harbored tubercle bacilli in necrotic tissue. What happened to large numbers of the present older generation earlier in life is still happening to survivors, namely, the unleashing of their tubercle bacilli, resulting in clinical disease. Present phenomenally low mortality rates in the younger age groups show the effectiveness of effort against tuberculosis which has resulted in protection against infection.

Morbidity

When at the opening of this century the mortality rate was in the neighborhood of 200 per 100,000 population, the number of clinical cases was only estimated. There probably were approximately 10 such cases for every death, a case rate of about 2,000 per 100,000 population. As mortality began to decline, there was a corresponding decrease in morbidity which had reached 48.8 per 100,000 in 1955. Several factors now operating could markedly change morbidity rates. Evidence is accruing to suggest that antituberculosis drugs do not have the permanent effect as was earlier predicted. Therefore, persons thought to have been "cured" are still harboring organisms which may still result in reactivations of old lesions and development of new ones. Indeed, this is already in evidence on a large enough scale to cause alarm.

Divergence of Mortality and Morbidity Curves

In 1920, the number of newly reported cases of tuberculosis in some places does not appear much higher than those in 1955. A casual glance at the figures could lead to an erroneous interpretation. The situation in 1920 was markedly different from that in 1955. In 1920, the vast majority of cases reported were sick people. They went to their physicians, clinics, etc. because of symptoms. This was before it was generally known that chronic tuberculosis usually passes through a long silent period when it can be detected, if sought, in apparently well people. If methods of finding the disease before symptoms appeared had been in practice in 1920, the number of cases reported that year could have been well-nigh doubled. By 1955, apparently healthy people were being examined for tuberculosis in the offices of physicians, in hospitals, clinics, and mass surveys, and many persons without symptoms were found with evolving disease and were reported. If only those who sought assistance because of symptoms had

been considered in 1955, the number of cases probably would have been less than half of the total number reported.

Since 1947, antituberculosis drugs have been used extensively and so suppressed tubercle bacilli that many tuberculous persons were still alive in 1955, who without these drugs would have died. Thus the number of such persons still living has increased. While mortality rates decreased precipitously, case rates declined as usual. Among infected persons, the annual crop of gross disease evolved just as it had in previous years. If a drug had been available which could have destroyed tubercle bacilli in the necrotic lesions from which new disease emanates, the case rate could have dropped as rapidly as the mortality rate. Without such a drug, as much gross disease developed percentage-wise among infected persons as at any time in history. The decrease in number of cases which did occur was the result of earlier control measures which reduced the incidence of infection. The smaller the number of infected persons, the fewer gross areas of disease develop.

Magnitude of Problem Not Determined by Mortality and Morbidity Rates

In determining the magnitude of the tuberculosis problem, mortality rates have never been satisfactory criteria for such reasons as: 1) Many persons who have known clinical and even contagious tuberculosis do not die from this disease; 2) Many with unrecognized clinical tuberculosis die from other acute and chronic conditions; 3) In recent years, antituberculosis drugs have at least postponed deaths from tuberculosis on a large scale, and thus mortality rates have decreased precipitously without significant change in other phases of the tuberculosis situation.

With the rapid decline in death rates from tuberculosis, obviously a sense of false security on the part of the public was sure to emerge. To overcome this situation, much emphasis has recently been placed on morbidity rates, which are less reliable than mortality rates. For example, reporting of clinical cases has rarely been satisfactory as evidenced by the number of which health departments are first notified by death certificates. Also, there is marked disparity in reporting. In some places only proved active clinical contagious cases are reported, while in other areas, almost any pulmonary abnormality is recorded as a case of tuberculosis. Mass x-ray surveys have resulted in much reporting of this kind. In 1955, in the United States, 78,618 new cases were reported under the category of active or probably active. Obviously, the probably active cases were not well documented in that tubercle bacilli were not recovered and the question as to how many of them were tuberculous is justified. It is well known that persons are still reported and sent to sanatoriums as tuberculous whose disease proves to be malignancy, sarcoidosis, etc. Recently, enough cases of pulmonary histoplasmosis were found in one sanatorium where they were being treated for tuberculosis to warrant the estimate of 1300 such cases now in sanatoriums in the histoplasmosis endemic area.[1] Among 24 persons being treated in a hospital for tuberculous pleurisy with effusion, thoracotomy and biopsy revealed that nine were nontuberculous.[2]

Accomplishments of Veterinary Profession

To date man's greatest victory over tuberculosis has been accomplished by the veterinary profession and its allies. Between 1890 and 1916, they acquired the fundamental information that made this achievement possible. Despite almost intolerable opposition at times, they pressed forward with a tuberculosis eradication program, which began in 1917. The year before, at the points of federal inspection, 40,746 cattle were condemned as inedible because of tuberculosis. In 1953, only 391 animals were so condemned, a decrease of 98.6 per cent. In 1916, one year before the nationwide eradication program began, enough cattle were condemned by federal inspectors to make a 15-mile solid train load of live cattle. In 1955, such animals could be accommodated in a train less than 0.3 mile long.

From 1917 to 1955, 369,606,820 tuberculin tests were administered to cattle of this country and the 4,034,297 reactors were slaughtered. The veterinarian's accomplishment has been phenomenal. By 1955 he had reduced the incidence of tuberculous infection among the cattle of America to 0.12 per cent. There is evidence to indicate that some of the relatively few animals which now become infected annually receive their tubercle bacilli from human associates rather than from other cattle. There are large areas in this country where no infected animal can be found.

The bovine type of tubercle bacillus was found capable of producing just as disabling and killing disease among people as the human type. In countries which have not controlled tuberculosis among the cattle herds, the bovine type of tubercle bacillus continues to wreak havoc among children and young adults, causing 50 per cent or more of all cases of tuberculosis of the skin and peripheral lymph nodes, 20 per cent of tuberculous meningitis and miliary disease, and 1 to 6 per cent of the cases of pulmonary tuberculosis.

Veterinarians have also done much to prevent tuberculosis in people by controlling it among other domestic animals and pets such as dogs, cats and parrots.

Wherever tuberculosis has been controlled among cattle there has followed definite decrease in infection attack rates, mortality and morbidity among people of the same areas.

A New Era Has Dawned

By the old definition, tuberculosis was considered present only when gross lesions were detectable by x-ray shadows, had resulted in illness, or tubercle bacilli were recoverable. All the stages in the evolution of the disease, from the initial invasion and focalization of tubercle bacilli to the presence of extensive disease, were ignored. Failure to find lesions in many tuberculin reactors by physical examination, including x-ray film inspection of the chest, led to the erroneous deduction that most reactors have infection but no disease. It was the minuteness and location of lesions that so long deceived physicians. Ghon[3] clarified this situation in the second decade of the present century by meticulous necropsies on the bodies of 184 persons who during life had no evidence of tuberculosis except the

tuberculin reaction. Detection of some of the pulmonary foci was "a very difficult task and often required considerable time." He also said, "The smallest foci were scarcely found at all in the cases with anatomical healing. This fact is of importance; it explains to us why it is often difficult to find such foci . . ." Ghon's observations, together with the vast post-mortem experiences of veterinarians in the United States on apparently healthy animals (more than 4,000,000) slaughtered because they reacted to tuberculin, leave no doubt that, where there is infection manifested by the tuberculin reaction, there are lesions. In reality, therefore, the tuberculin reactor has tuberculosis.

This is the era of eradication of the tubercle bacillus. In the past, most funds, time, and effort have been spent on finding and trying to repair damage produced by the tubercle bacillus. When the 20th century opened, such inroads had been made by this disease that the ill and the dying demanded every attention that could be mustered. The work was done so well and the disease is now so in hand that the era of tubercle bacillus hunting and destruction is upon us. The medical profession and its allies are now in possession of all the necessary information and have at hand the armamentarium to eradicate tuberculosis.

When Tuberculosis Begins

The evolutionary processes from the initial invasion of the human body with tubercle bacilli to death of their victim are known. In the earlier years of effort against this disease it was thought to begin when symptoms were first in evidence. This opinion had prevailed since the days of Hippocrates. With the extensive use of the x-ray film, beginning in the early 1920's, many persons were seen who had shadow-casting lesions which later proved to be tuberculous, yet symptoms were absent. Therefore, it was said that the x-ray film finds tuberculosis at its beginning. Later, extensive and prolonged observation showed that x-ray shadows often do not appear until years or decades after the disease has been present, and in a great many people the x-ray film never reveals evidence of disease, although it is present in abundance.

Experimental work has shown that tuberculosis begins within an hour after the invasion of tubercle bacilli. In that time organisms introduced directly into the blood streams of animals have been phagocytosed by white blood cells (neutrophils) and focalized.

Focalization and subsequent tubercle formation occurs in many places in the body simultaneously. Some may be in the brain, spleen, liver, kidneys, bones, joints, etc. More are likely to lodge in the lungs than anywhere else because of their numerous small capillaries. Thus the established microscopical foci of tubercle bacilli are multiple and any one or more of them may at some subsequent time result in destructive disease.

Diagnosis

During the first weeks of the existence of tuberculosis, the tissues of the body including the skin become sensitive to tuberculoprotein. This sensitivity, also known as allergy, can be detected by the reaction to tuber-

culin within three to seven weeks after the initial invasion of tubercle bacilli. The sensitivity of the tissues persists as long as tubercle bacilli remain alive in the body. Therefore, by the tuberculin reaction the physician diagnoses tuberculosis while lesions are still microscopical.

In many persons who develop these minute lesions, the disease never progresses to clinical proportions. However, everyone who does develop clinical disease passes through the stage when no phase of the most complete examination reveals its presence except the tuberculin reaction.

The old theory that persons with tuberculous infection as manifested by sensitivity to tuberculin walk in a charmed circle of safety, has been replaced by the fact that such persons walk within the circle where all illness and death from tuberculosis occur.

As yet, we have no way to determine which persons who react to tuberculin will at some subsequent time develop clinical disease. Therefore, everyone who is found to be a reactor should have those parts of the body which clinical tuberculosis frequents examined periodically. If the individual is in infancy, the parents should be instructed to inform the physician at once if symptoms appear suggestive of miliary or meningeal tuberculosis.

If the individual is in early childhood, one must watch for extrathoracic lesions, particularly those of bones and joints, and especially the spine, hip and knee joints. Only rarely does chronic pulmonary tuberculosis develop in children. Among individuals approaching adolescence or who are in later periods of life, including old age, the lungs must be examined periodically. Throughout adulthood, 10 to 15 per cent of clinical tuberculosis develops extrathoracically.

Inasmuch as 85 to 90 per cent of clinical tuberculosis develops in the lungs of adults, it is important that every adult tuberculin reactor be alerted to the necessity of periodic examinations. However, these should always include but never be limited to x-ray inspection of the chest.

By x-ray film inspection one is able to detect chronic gross clinical lesions earlier in their evolution than by any other phase of examination. These chronic lesions usually evolve slowly so six to 12 months intervals between examinations are adequate. Among those persons in whom such lesions are destined to evolve, they can often be found by the shadows they cast long before symptoms appear and before they are contagious. As yet, we have no method of preventing such lesions from evolving in a considerable percentage of infected persons and, obviously, our only recourse is to find them as early as possible.

Values of the Tuberculin Test

1. When the disease is found by the tuberculin test as soon as the tissues have become sensitized, one has made the earliest possible diagnosis of tuberculosis. This is usually long before symptoms or x-ray shadows are in evidence, or contagion is present. Knowing that tuberculous lesions containing tubercle bacilli, even though microscopical, are present places the physician on the alert and makes it mandatory that the individual, regard-

less of age, be kept under close observation for the earliest possible evidence of clinical lesions that may evolve.

2. Finding tuberculosis soon after allergy appears enables the physician and the health officer to locate the source of the infection in adult associates much more often than by any other method. There is nothing more fascinating in medicine than picking up the trail of tuberculosis by the tuberculin test and following it to its headquarters in the body of a person or an animal.

3. By finding tuberculosis promptly after allergy appears the physician and the courts should be able to place responsibility for the individual's infection. In many places tuberculosis is now compensable for such groups as industrial workers, students, interns, residents and other employees of hospitals. The industry or institution that permits its employees, students, or other personnel to be infected in line of duty is in reality responsible for the clinical tuberculosis which may subsequently develop.

4. Keeping persons recently infected under observation by periodical examinations enables the physician to find those destined to develop clinical reinfection type of pulmonary disease while lesions are small, before they have caused symptoms or become contagious and when they can be treated successfully. Moreover, it is possible that the tuberculin test may determine the time to treat tuberculosis with antituberculosis drugs, with the hope of actually curing the disease and thus avoiding much destruction of tissue, illness, or death. This refers to recent converters whose lesions are microscopical and vascular. It depends upon whether present or future drugs prove to be germicidal. If so, in such cases, the tuberculin test may determine when sufficient treatment has been administered. When all bacilli have been destroyed, the individual's tuberculin sensitivity should revert.

5. The tuberculin test determines the magnitude of the tuberculosis problem in any group of people since it readily detects those who are harboring tubercle bacilli, and it is they who constitute the problem.

6. The effectiveness of a tuberculosis control program can be determined accurately and with reasonable promptness only by the tuberculin reaction. Testing all with tuberculin before the program starts fixes the base line. Five years later testing the children born since the program began determines whether they have been better protected than those of the same age preceding the program.

The Present Problem and Its Solution

Tuberculosis constitutes an important item in our national defense.[4] There is no other major disease with such a strong foothold among our citizenry. Failure to take full cognizance of this fact in World Wars I and II, the Korean War, and other military activities proved extremely destructive to those involved and to the nation.

Tuberculosis is said to be costing this country $600,000,000 annually. If all costs were considered, including loss of time of patients and deaths, the actual amount would be at least five times this estimate.

In 1954, 16,392 of our citizens died and in 1955, 78,618 active or probably active new cases of tuberculosis were reported.

If eradication is to be our goal, locations of tubercle bacilli must be known and the attack begun against them. If we continue to consider only the mortality rate of approximately 10.2 per 100,000 or the "case" rate of about 48.8 per 100,000, with an estimate of 500,000 "cases" in the entire country, eradication will never be achieved. The numbers of deaths and so-called cases being reported annually are no longer enough to insure continuing interest and support of the public in this disease. If the estimate of 500,000 so-called cases were accurate, it represents only approximately 3/10 of 1 per cent of our entire population.

Our sights must be raised and precise aim taken at the tubercle bacillus rather than the gross disease it produces. The only unerring method of determining the magnitude of our present and future situation consists of determining where the remaining tubercle bacilli are by finding with the tuberculin test those who are harboring them. Although testing has been extremely limited, particularly among older adults, enough has been done to indicate that approximately one person in three is now harboring tubercle bacilli. Each one of these persons, regardless of apparent good health or clarity of x-ray films of the chest, has areas of disease containing tubercle bacilli. Thus, in the strict sense of the word, each one is a case of tuberculosis, and many who do not already have gross areas of disease will have such lesions evolve before their spans of life are completed. Therefore, we should now inform our citizenry that the case rate is 30,000 per 100,000 of our population. The exact rate for each area can be determined only by testing the entire population with tuberculin. In some counties in the upper midwest where such testing has been done, the case rate has been found to be 22,000 per 100,000. There are probably areas where a lower rate obtains, and most likely there are parts of states, particularly large cities, with definitely higher rates.

Only Successful Methods

In those parts of the world where tuberculosis has been so dramatically reduced over the last few decades, certain operations against the disease have been almost universally employed. These have consisted of good diagnostic work, isolation of contagious cases, best available treatment, and protection against the bovine type of bacillus. This result also is seen in parts of the same countries or certain population segments, notably those hospitalized for mental illness and the American Indians, where tuberculosis was rife until the above factors were introduced.

Wherever the above procedures have been even reasonably well operated for the past few decades, their effectiveness has been so apparent that such areas now stand in bold relief on the world map. It appears to have made no difference how little or how much else was done. Moreover, in parts of the world where these procedures were not in operation but other methods were employed, the decrease in tuberculosis has not been outstanding.

Methods that have been responsible for such marked reduction in

tuberculosis and which probably are adequate to eradicate the disease are now on such sound footing that the medical profession around the world can take a cue from them.

Physicians Must Take Initiative

Physicians should promptly assume leadership since they must do the diagnostic and therapeutic work. However, the solution of the problem will require every possible ally as Osler indicated in a "last word message" to the general practitioner. "The leadership of the battle against this scourge is in your hands. Much has been done, much remains to do. By early diagnosis and prompt, systematic treatment of individual cases, by striving in every possible way to improve the social condition of the poor, by joining actively in the work of the local and national antituberculosis societies you can help in the most important and the most hopeful campaign ever undertaken by the profession."

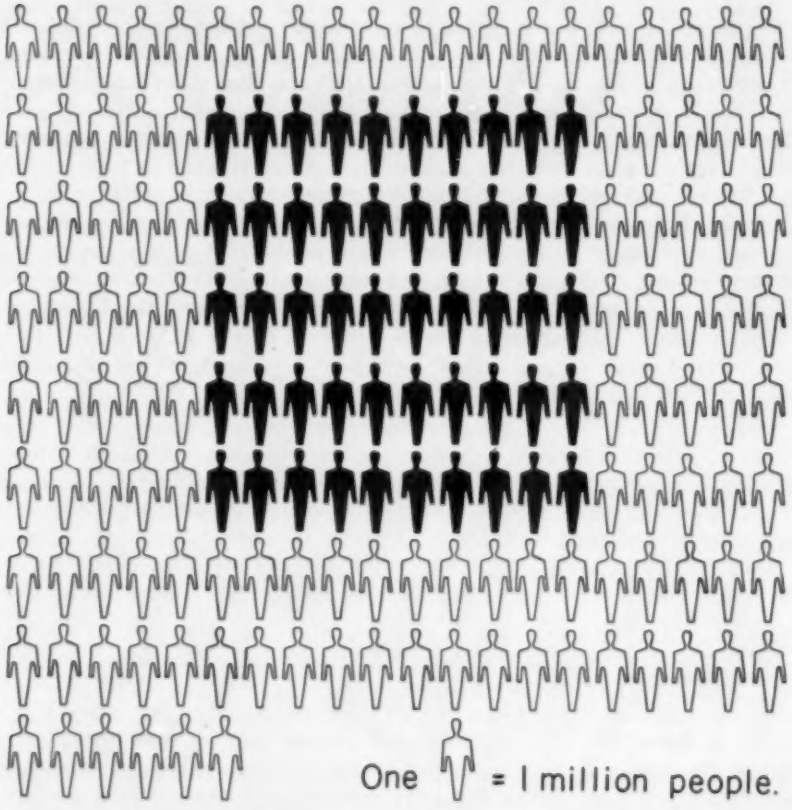

FIGURE 1: Each of the 166 figures represents a million persons. On the basis of the small amount of tuberculin testing done it is estimated that about 30 per cent (shown in black) of our 166,000,000 people are harboring tubercle bacilli.

Our allies must be supported to the nth degree. They include every citizen. Lack of information about tuberculosis, misunderstanding, and the like have resulted in complacency on the part of many individuals and even organizations. Just now, this is resulting mainly from the marked decreases in mortality and morbidity. Never in history has such a powerful and effective group of people banded together to fight a single disease as those of the National Tuberculosis Association with its 3,000 component state and local societies. This organization delivers messages to the people in every nook and cranny of this country. More than any other group, it is qualified to inform our citizenry of the magnitude of the tuberculosis problem which is less than half solved. Dissemination of such information is essential if physicians are to have complete cooperation in conducting the necessary professional work.

Tuberculin testing the 166,000,000 citizens in this country is well within the realm of physical possibility, and it is essential if eradication of the tubercle bacillus is our goal (Figure 1).

The program now becomes one of refinement in tracking down tubercle bacilli and keeping them corralled. The magnitude of the problem demands greater activity than has yet been seen in the tuberculosis eradication movement. It will require larger funds and more workers, as the entire citizenry must be informed to insure cooperation in the fight against the tubercle bacillus rather than just the damage it causes. Nurses and physicians everywhere, and particularly those in general practice, must be in the campaign. Indeed, they will need to do the lion's share of the work, and they are capable of doing it. There are over 200,000 physicians in this country, of whom 90,000 are in general practice. Trudeau's appraisal (1905) "On the general practitioner and the dispensary physician rests a great responsibility of detecting the disease in its incipiency. It is to them and not to the specialist that the patient first applies" is as applicable today as when it was written.

There are more than one-half million registered nurses in the United States who can do a large volume of work. In physicians' offices and clinics, nurses give hypodermic injections and intradermal tests. There is no reason why they should not administer tuberculin tests in a national program. In fact, they have already been assigned this responsibility and are carrying it out in many places in this country. With good organization and some experience, one person can administer 300 intracutaneous tuberculin tests per hour with ease.

When tuberculin testing is done, reactors need to be examined, including x-ray film inspection of chests of adults, not forgetting that 10 to 15 per cent of all clinical tuberculosis develops extrathoracically. Among tuberculin reactors one would expect 1 per cent or less to show evidence of clinical disease on first examination. Some of these persons are already contagious and need to be managed accordingly. Others have evolving lesions that have not yet become contagious which can be promptly controlled. The remaining 99 per cent have lesions, but most of them are

not now large enough or do not have the consistency to cast visible x-ray shadows. Some have lesions which are located in the 25 per cent of the lungs not visualized on usual films, and in others lesions are located extrathoracically.

From this 99 per cent an annual crop of evolving clinical lesions will have to be harvested. This necessitates periodic examinations of all reactors. Laments of tuberculosis workers have long been heard because such a high percentage of persons had the disease in an advanced stage when first found. Among the 78,618 active or probably active cases reported in the United States in 1954, 78 per cent were in an advanced stage (Figure 2). The solution of this problem consists of finding the individuals who are harboring tubercle bacilli and examining them periodically. This has been done in sufficient volume and over long enough time to leave no doubt as to its efficacy. It results in finding 95 per cent of chronic lesions destined to evolve while they are minimal, before they have caused symptoms, before they are contagious, and when nearly all can be treated successfully and returned to usual activities of life in a relatively short time (Figure 3).

Children and adults alike who have not been infected and therefore do not react to tuberculin must be retested periodically. Among those who are found to convert to tuberculin reactors, destruction of all their bacilli with antituberculosis drugs may become possible. If not, they must be reexamined periodically like those who reacted on first examination.

Precedents Established

The medical profession is now in position to render an outstanding public service. Already in a few places physicians have demonstrated their

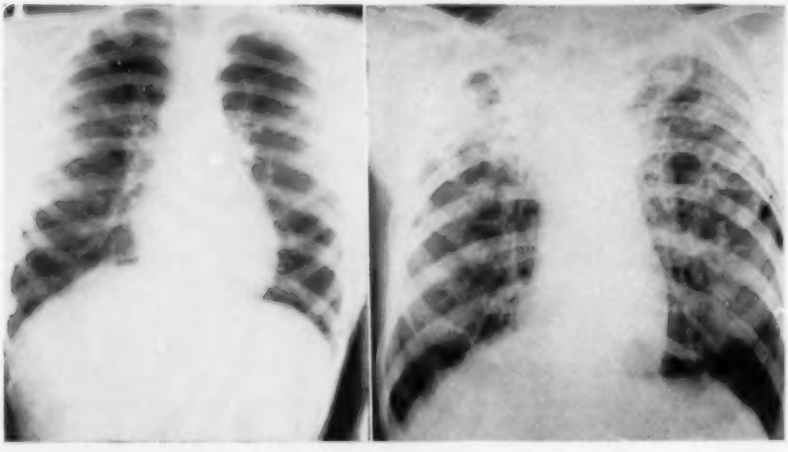

FIGURE 2: When the tuberculin reaction is ignored. *A*. From roentgenogram taken December, 1923 of chest of a 12 year old girl. No evidence of significant shadow-casting lesion. Annual film inspection for five years. No change. Thereafter connotation of tuberculin reaction ignored. *B*. From roentgenogram taken June, 1947 of same chest after symptoms appeared. Lesions proved to be those of advanced contagious and fatal pulmonary tuberculosis.

ability to contribute such service. In Meeker County, Minnesota, in 1941 the medical society set out to control tuberculosis. They instituted a county-wide demonstration. During this demonstration period, they made the necessary time and effort a gift to the citizenry of the county. No charge was made for administering and reading the tuberculin test, exposing, developing, and reading x-ray films, or completing examinations when indicated. This demonstration revealed that about 22 per cent of the citizens, mostly older people, were harboring tubercle bacilli. Among them, 16 were found to have clinical tuberculosis.

This public service greatly increased the confidence of the citizenry in its medical profession. It demonstrated that local physicians are capable of doing modern tuberculosis work. It squelched those who believe and teach that physicians are interested only in fees.

During the demonstration period, the public was informed that all persons who did not react to tuberculin should have the test repeated at least annually, while all who reacted then or subsequently should be examined at least once a year for the detection of clinical lesions which might evolve. Ever since the demonstration closed, a great many people from Meeker and adjacent counties have gone periodically to physicians' offices and hospitals as private patients to have tuberculin tests, x-ray films, or whatever was recommended.

The physicians of three other counties in the same state have since conducted such demonstrations. Another has just been completed in Hastings, Minnesota, with a population of approximately 7,000. There 90 per cent of the entire citizenry responded for tuberculin testing which was done without charge by the local medical profession. X-ray films of chests of reactors were exposed, developed, and read at cost.

Another excellent example of such work is that of the St. Louis Academy

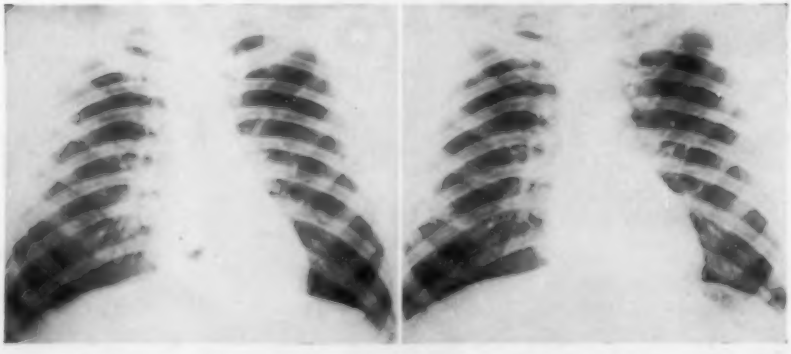

FIGURE 3: When the tuberculin reaction is heeded. *A*. From a roentgenogram taken August, 1945 of the chest of a man of 22 years. At age 14 he reacted to tuberculin. Annual x-ray films of chest including this one were clear. *B*. From roentgenogram December, 1946. Note small shadow-casting lesion left apex. Tubercle bacilli recovered from stomach washings. Brief period of treatment. No manifestation of clinical tuberculosis since. Nearly all chronic pulmonary tuberculosis can be found in this stage by periodically examining tuberculin reactors.

of General Practice with approximately 200 members. In 1951, this Academy adopted tuberculin testing in schools as its main project. This has since been in continuous operation as a public service with 100,000 tests having been administered as of January 1, 1956. Examinations have been completed as indicated and sources of children's infections have been sought with considerable success.

The question is not whether physicians can afford to conduct demonstrations gratis but rather that they cannot afford to overlook such opportunities. It is an excellent way of securing and maintaining confidence, good will and support of the citizenry. These are the factors which are so needed in returning the greater part of the tuberculosis problem to the offices of local physicians, particularly those in general practice. When this is accomplished, we may expect the most effective attack of all time upon the tubercle bacillus.

Special Techniques to Hasten Eradication

Spot Maps. By tuberculin testing the people of any area are promptly divided into two groups: those who are and those who are not harboring tubercle bacilli. This places the subsequent attack on tuberculosis on a scientific and practical basis. The percentage of tuberculin reactors varies

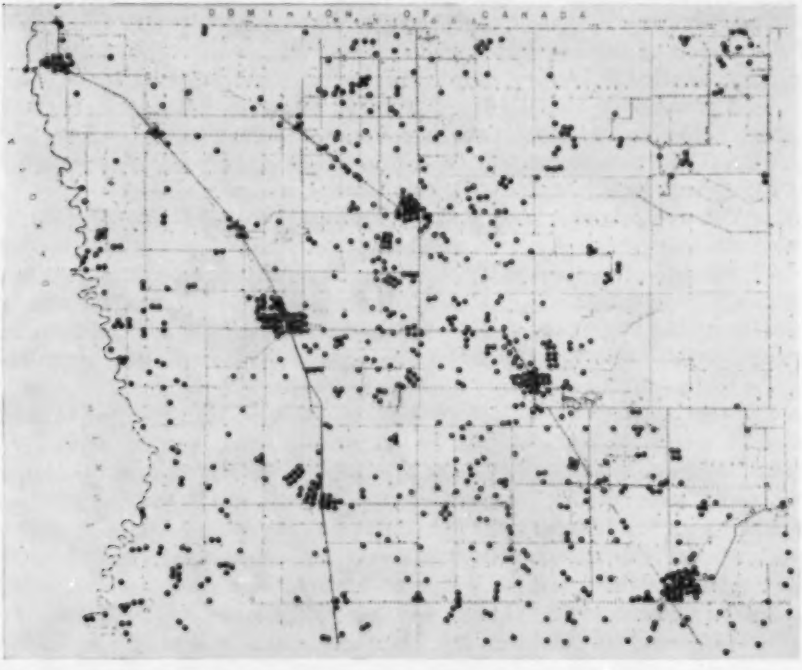

FIGURE 4: Map of Kittson County, Minnesota, a so-called tuberculosis low incidence area. Dots indicate the residents of persons harboring tubercle bacilli as manifested by the tuberculin reaction.

somewhat from place to place. There are probably entire counties where not more than one-fifth of the individuals, mostly in the upper age bracket, will react to tuberculin. There are other areas where 40 per cent or more may be infected, and likely the average for the nation is about one in three.

Formerly spot maps were produced indicating with thumbtacks where persons had died from tuberculosis. Later maps were made to show where clinical cases had been found. Now a map should be made for each of the 3,070 counties in the United States showing where each person resides who is harboring tubercle bacilli as manifested by the tuberculin reaction. Miss Mary Goddard, Public Health Nurse, Kittson County, Minnesota, in cooperation with the local medical profession, the State Department of Health, and the State Tuberculosis and Health Association has produced such a map (Figure 4). She and coworkers know where tubercle bacilli now reside in that county. Moreover, they know how to keep them corralled. Kittson is a county of so-called low tuberculosis incidence since three "new cases" were reported and one died in 1954. Indeed, there were only 13 persons currently registered as having tuberculosis. Nevertheless, 2,100 persons still harbored tubercle bacilli among Kittson County's population of 9,600. In contrast, among the 15,526 cattle of the county, no tuberculin reactor was found in 1954.

Certification of Schools. Techniques already in operation in several states will hasten the solution of the problem. For example, the Committee on Tuberculosis of the American School Health Association (A. O. DeWeese, M.D., Executive Secretary, Kent University, Kent, Ohio) has devised a method of working in schools which consists of officially certifying individual and groups of schools that meet standard qualifications. As schools qualify, the certificates are signed by the president and executive secretary of the American School Health Association, the executive secretary of the State Tuberculosis and Health Association, and the chairman of the state subcommittee of the American School Health Association. This project, which has been in operation for a decade, stimulates interest and activity in tuberculosis eradication not only in the schools but in the entire community supporting them. It is not unusual for every person in the community to be examined for tuberculosis before the project is completed. It has spelled the doom of the tuberculous teacher, bus driver, etc., as well as students, particularly those of high school age, transmitting tubercle bacilli to personnel and students. Its educational value is immense.[5]

In 1954 there were in the United States more than 16,000,000 pre-school children. From five to 14 years inclusive, there were 27,118,000 children, and from 15 to 19 years, 12,854,000. There were more than 1,000,000 professional and approximately 200,000 non-professional employees in the schools of this country. The best kind of education comes through actual participation of children and personnel alike. Opportunities are unlimited among the children and the personnel members of our schools. This group, which constitutes nearly one-third of our total population, can promptly be converted into a mighty army against tuberculosis as its members learn about the disease by participating in school programs.

Program Economically Sound

The soundness of this program economically is beyond question. Although additional funds are necessary to locate the tubercle bacilli and to keep them corralled, many times the immediate initial cost will be saved in reduced illness, death, etc., in both animals and people. A good example is the eradication program among cattle. It cost the owners of these animals $300,000,000 every ten years prior to the initiation of the national eradication program. It cost only $260,000,000 to reduce the disease so each state qualified for modified accredited rating. The present cost of the program, which is rapidly approaching eradication of this disease, is a mere fraction of what it was in the beginning. This country no longer has to expend vast sums of money in reimbursing owners of cattle for those condemned to rendering tanks. Funds are now being spent more profitably to test and retest animals periodically and thus find most of those that have become infected before the disease is contagious and when little loss is suffered by owners.

Among humans, caring for the ill and dying will gradually be obviated and thus money and personnel can be transferred to more refined activities. Chronic pulmonary lesions that are detected as soon as possible after they start to evolve require much shorter periods of treatment than those of long duration and many of them do not need hospitalization. Most of them can be prevented from becoming contagious and thus the tubercle bacillus cannot perpetuate itself in other human and animal bodies.

The Goal

The ultimate goal is eradication of tubercle bacilli. Unless some method of destroying these organisms in avascular lesions in living tissues is devised, eradication of these organisms will be accomplished only by keeping them corralled in the bodies of people who now possess them as long as these individuals live. Thus, if from this moment no more new infections occurred, eradication is as far away in point of time as the death of the last person now harboring tubercle bacilli. It is true in this country that the vast majority of tubercle bacilli have taken refuge in the bodies of older people who will die within the next few decades. With their passing there will remain the relatively few infected persons who are now younger but in whose bodies bacilli must be kept corralled for the remainder of their lives.

Infants infected today may remain in good health through long lives but still may become clinical and contagious cases of tuberculosis in senility from progeny of tubercle bacilli which invade their tissues today. Thus, if infants are infected now, the tuberculosis eradication goal is no nearer than it was when this century began.

Eradication of tubercle bacilli must apply to the three now known pathogenic types—human, bovine, and avian. Each of them produces clinical disease in more than one species of animals and all cause such disease in people. It is of little avail to eradicate the human type with the others extant and vice versa. Therefore, it is important that the medical profession

cooperate with the veterinary medical profession in the all out eradication movement.

Although veterinarians and their allies are approaching the bovine eradication goal and have attained it in many places, they continue to tuberculin test the entire cattle population of this country periodically. A. G. Karlson, D.V.M., Mayo Foundation, says: "An animal that reacts positively to the tuberculin test is properly considered as a dangerous individual . . . in spite of the great advances in control, there is a constant potential hazard as long as only a few infected animals exist." This statement is equally true of people.

We must agree with David T. Smith, M.D., Duke University, when he says that even in this country where so much has been accomplished, we have not even reached the halfway mark in our eradication program. The more difficult and laborious work remains to be done. Any tuberculosis association that sets eradication as its goal and is willing to do the necessary work will have plenty to do throughout the lifetime of every person now engaged in the work. Much will remain to be done by our successors.

Just as we strove through the decades of this century to drive downward the mortality rate from about 200 and the morbidity rate from 2,000 per 100,000, we must new strive to drive downward the case rate of approximately 30,000 per 100,000 population. Our future success must be measured in reductions of this real case rate, and the goal will not be reached in any community or state until there is no case of tuberculosis manifested by the tuberculin reaction.

SUMMARY AND CONCLUSIONS

In some parts of the world tuberculosis is now so well under control that its eradication is contemplated.

Here lies one of the great opportunities of the medical profession which possesses information and armamentarium to accomplish this goal.

With the tuberculin test all persons harboring tubercle bacilli can be identified. They have multiple lesions, some of which are large and can be located but most of which are microscopical. X-ray film inspection of chests reveals gross lesions but misses all others. Among the tuberculin reactors with clear x-ray films, many will have gross lesions evolve later. Therefore, periodic x-ray film inspections of their chests are necessary to harvest this crop while the lesions are minimal, asymptomatic, non-contagious, and most treatable. When periodic examinations are not done, late harvest yields a preponderance of advanced cases.

Tuberculin reactors have multiple tuberculous lesions even though they are well and present clear x-ray films of their chests. In reality, each reactor is a case of tuberculosis and must be managed as such to keep his tubercle bacilli corralled.

If tuberculosis eradication is desired, each community, county, and state should locate the existing tubercle bacilli which are in the bodies of people and animals who react to tuberculin and act accordingly.

Physicians must do the diagnostic and therapeutic work. Thus, they should initiate and perpetuate such work everywhere. Cooperation with all organizations and individuals is essential to insure community-wide participation. Precedents have already been set by medical organizations. Private offices of physicians can constitute our best tuberculosis eradication centers.

Tuberculosis eradication is a national defense measure, and the opportunity to accomplish it should not be overlooked by the medical profession.

RESUMEN Y CONCLUSIONES

En algunas partes del Mundo la tuberculosis se encuentra tan bien controlada que su erradicación ya puede avizorarse.

Esta es una de las oportunidades de la profesión médica que posee la información y el equipo para llegar a este objetivo.

Con las pruebas de tuberculina todas las personas que tienen en su organismo bacilos de la tuberculosis puede descubrirse.

Ellas tienen lesiones múltiples, algunas de las cuales son grandes y pueden localizarse, pero la mayoría son microscópicas.

La búsqueda por los rayos X, revela las lesiones grandes, pero omite el descubrimiento de otras. Entre los reactores a la tuberculina con películas radiológicas limpias, muchos tendrán lesiones gruesas más tarde. Por tanto, es necesaria la inspección periódica del tórax para sorprender las lesiones en su etapa mínima, asintomática no contagiosa y más tratable.

Cuando no se hacen exámenes periódicos las investigaciones más tarde rinde un volumen con preponderancia de casos avanzados.

Los reactores tuberculínicos tienen lesiones múltiples aunque estén bien y tengan radiografías normales. En realidad todo reactor es un caso de tuberculosis y como tal debe ser tratado paramantener sus bacilos acorralados.

Si se desea obtener la erradicación de la tuberculosis, toda comunidad, condado o estado debe localizar el bacilo tuberculoso que se encuentra en los cuerpos de los hombres y de los animales que reaccionan a la tuberculina y debe actuarse sobre él.

Los médicos deben hacer el trabajo terapéutico y diagnóstico.

Así ellos deben iniciar y mantener tal trabajo en todas partes.

La cooperación con todas las organizaciones e individuos es esencial para asegurar una participación en toda la extensión de la comunidad. Ya hay precedentes establecidos por organizaciones médicas. Los consultorios privados de los médicos pueden constituir los mejojres centros de erradicación.

La erradicación de la tuberculosis es una medida de defensa nacional y no debe pasarse por alto esta oportunidad por parte de la profesión médica.

RESUME

Dans quelques parties du monde, la tuberculose est si bien jugulée qu'on peut penser à son éradication.

Ici réside l'une des plus belles actions du corps médical, que possède les données et l'armement nécessaires pour arriver à ce but.

Avec la tuberculine, tous les individus porteurs de bacilles de Koch peuvent être identifiés. Ils ont des lésions multiples, quelques-unes sont très importantes, et peuvent être localisées, mais la plupart d'entre elles sont microscopiques. L'investigation radiologique des thorax décèle les lésions grossières, mais laisse échapper toutes les autres. Parmi les individus qui réagissent à la tuberculine, avec des radiographies normales, plusieurs auront des lésions importantes qui évolueront ultérieurement. C'est pourquoi les examens radiologiques systématiques sont nécessaires pour faire la moisson de ces cas alors que les lésions sont encore minimes, asymptomatiques, non contagieuses, et la plupart du temps curables. Quand les examens systématiques ne sont pas faits, la moisson suivante apporte une prépondérance de cas avancés.

Les individus réagissant à la tuberculine ont des lésions tuberculeuses multiples même s'ils sont bien portants et si leurs radiographies thoraciques sont normales. En réalité, chaque individu réagissant à la tuberculine est un tuberculeux, et doit être considéré à ce titre comme un réservoir de bacilles.

Si l'on désire l'éradication de la tuberculose, chaque communauté, région et état, devraient localiser les bacilles tuberculeux existant dans le corps des individus et des animaux qui réagissent à la tuberculine, et agir en conséquence. Les médecins doivent faire le diagnostic et le travail thérapeutique. Ensuite, ils devraient introduire et perprétuer partout cette activité. La collaboration de toutes les organisations et des individus est capitale pour assurer une large participation de la communauté. Des précédents ont déjà été créés par des organisations médicales. Les cabinets privés de consultation peuvent constituer nos meilleurs centres d'éradication de la tuberculose.

L'éradication de la tuberculose est un moyen de défense nationale et sa réalisation ne devrait pas être sousestimée par l'ensemble du corps médical.

ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNGEN

In einigen Teilen der Welt steht die Tuberkulose heute so gut unter Kontrolle, dass ihre Ausrottung diskutiert wird.

Hier liegt eine der grossen Chancen für den ärztlichen Beruf, der Kenntnis und Rüstzeug besitzt, um dieses Ziel zu erreichen.

Mit Hilfe des Tuberkulin-Testes können alle Personen, die Tuberkelbakterien beherbergen, erfasst werden. Bei ihnen finden sich mannigfache tuberkulöse Veränderungen; bei einigen sind diese Veränderungen gross genug, um lokalisiert werden zu können, aber bei den meisten sind sie nur von mikroskopischer Grössenordnung. Die Röntgen-Untersuchung des Thorax lässt nur ausgedehntere Veränderungen erkennen, aber ergibt bei allen anderen kein Resultat. Unter den Tuberkulinpositiven ohne Röntgenbefund werden sich später bei vielen sich bare Veränderungen entwickeln. Deshalb sind periodische Röntgen-Untersuchungen erforderlich, um diese Prozesse zu erfassen, solange sie noch am wenigsten ausgedehnt, symptomlos, nicht ansteckend und mit besten Aussichten behand-

lungsfähig sind. Wenn solche regelmässigen Kontrollen nicht durchgeführt werden, dann wird späterhin die Zahl der fortgeschrittenen Fälle überwiegen.

Tuberkulinpositive haben multiple tuberkulöse Veränderungen, selbst dann, wenn sie sich gesund fühlen und einwandfreie Röntgenbilder bieten. In Wirklichkeit ist jeder Tuberkulinpositive ein Fall von Tuberkulose und muss als solcher betrachtet werden, um den Ausbruch einer fortschreitenden Erkrankung zu verhindern.

Wenn die Ausrottung der Tuberkulose angestrebt wird, sollte jede Gemeinde, jeder Kreis und jedes Land bemüht sein, die Lokalisation der Tuberkelbakterien bei Menschen und Tieren, die tuberkulinpositiv reagieren, zu erfassen und die notwendigen Massnahmen einleiten.

Die Ärzte müssen die diagnostische und therapeutische Arbeit leisten. Es sollte daher überall eine derartige Arbeit begonnen und fortgeführt werden. Die Zusammenarbeit mit allen Organisationen und Einzelpersonen ist erforderlich, um eine wirklich umfassende Teilnahme der Gemeinden zu sichern. Die Voraussetzungen sind schon durch die ärztlichen Berufsorganisationen geschaffen. Die Praxen der niedergelassenen Ärzte können unsere besten Tuberkulose-Ausrottungs-Zentren werden.

Die Ausrottung der Tuberkulose ist eine nationale Abwehrmassnahme und die günstige Gelegenheit zu ihrer Durchführung sollte vom Ärztestand nicht übersehen werden.

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The Results of Mitral Commissurotomy One to Three Years After Surgery

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Although generally favorable results have been reported in selected cases treated by mitral commissurotomy, the question of long range benefit remains to be evaluated. After the passage of several years, a more realistic evaluation may be made since the initial enthusiasm of both patient and physician has time to react with factual experiences. Furthermore, the defect in the valve produced by the surgeon will have effected a more finite physiological and anatomical equilibrium.

We have re-evaluated an unselected group of patients after an interval of 12 to 36 months following surgery. Criteria for surgery have been previously described.[9] Since evaluation of functional improvement must be based on the symptoms of fatigue and dyspnea which are easily influenced by many extraneous factors, we have also studied less easily influenced symptoms such as paroxysmal nocturnal dyspnea and hemoptysis. Whenever possible, we have applied the objective measurements of pulmonary artery pressure by cardiac catheterization, electrocardiograms, x-rays, and physical examination in comparing the preoperative status with the condition at the time of follow-up.

Materials

Fifty-six patients were operated upon at the Los Angeles County Hospital between April, 1951 and September, 1953 with the intention of performing mitral commissurotomy. The procedure was not completed in seven patients for the following reasons: In four instances too much mitral regurgitation was present; one patient's pulmonary function was too poor after thoracotomy; another patient developed pulmonary edema early in the procedure; and one patient died before the pericardium was opened. Of the remaining 49, five had died before the time of completion of this study in October, 1954. We succeeded in re-examining or obtaining detailed follow-up studies on 32 of the 44 who had survived commissurotomy for from 12 to 36 months. Seventeen were in the second postoperative year and fifteen were in the third. Thirty of these patients had been studied by cardiac catheterization prior to surgery and 18 were restudied by catheterization after surgery. In four instances the recatheterization studies were done during the first half year following surgery and during the second half year in five instances, during the second postoperative

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TABLE I
IMPROVEMENT IN FUNCTIONAL CAPACITY

Right Ventricular Systolic Pressure Group	Reduction in Classification 0	1	2	3	Total Cases
I (30 - 45 mm.)	3	4			7*
II (46 - 80 mm.)	1	12	1		14
III (over 80 mm.)		7	1	1	9
A (no cath.)	1			1	2**
TOTAL	5	23	2	2	32

* 2 cases for emboli only
** 1 case for emboli only

year in six instances, and during the third postoperative year in three.

At the time of surgery five were in the third decade of life, fourteen in the fourth, nine in the fifth, and four in the sixth.

In three the indication for surgery was repeated peripheral emboli. In 13 the indication was disability severe enough to prevent the lightest household tasks or sedentary occupation. In the remaining 16 there was less functional impairment but the disability was progressive.

Results, Subjective

Functional capacity was assessed by detailed questioning in respect to typical household, occupational, and recreational tasks. The patients were graded in the classes of functional capacity by the criteria of the American Heart Association. Comparing the preoperative classification with functional classification at the time of follow-up gave us a somewhat more objective understanding of improvement than accepting a statement of change in the patient's own words. Such statements usually proved to be more optimistic than warranted. As is known[1] there are pitfalls in any such subjective evaluation. This was vividly brought to our attention when we discovered that a patient who had been evaluated as showing minor but definite improvement had been merely explored without manipulation of the valve because marked insufficiency had been found at surgery.

TABLE II
CHANGE IN RIGHT VENTRICULAR PRESSURE

Group	No. of Cases	Per Cent of Preoperative Pressure: Reduction <10	10 to 20	20 to 40	40 to 60	60 to 80	Increase 25
I	5	2	2	1			
II	8	3	2	1	1		1
III	5			1	3	1	

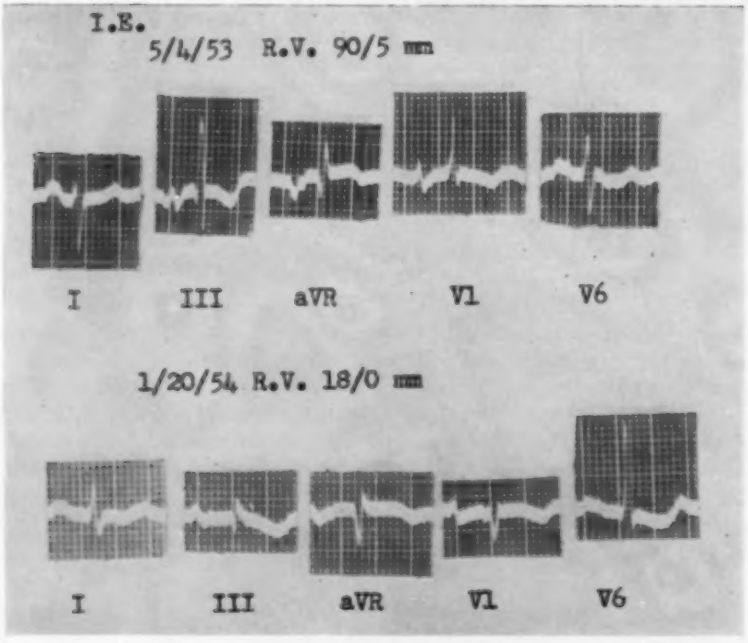

FIGURE 1A

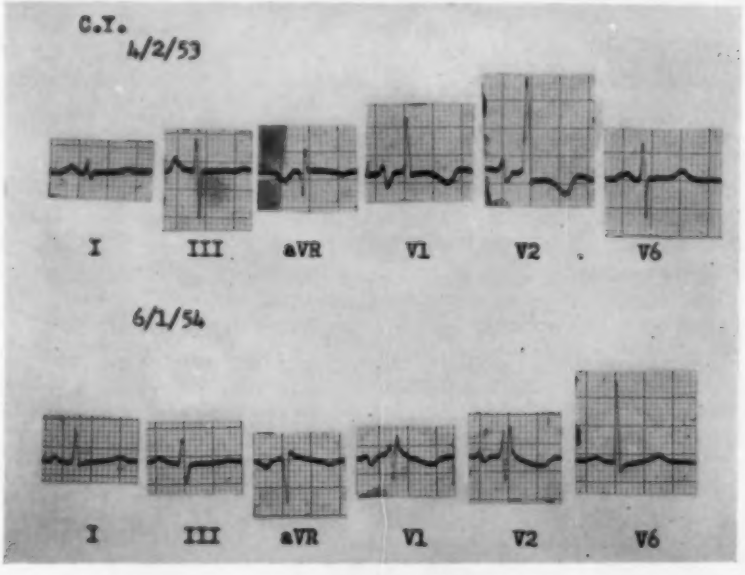

FIGURE 1B

Figure 1: Preoperative electrocardiograms and follow-up electrocardiograms in two patients showing marked change in the pattern of right ventricular hypertrophy. (a) Eight months after surgery. (b) Fourteen months after surgery.

TABLE III
RIGHT VENTRICULAR PRESSURE
vs
FUNCTIONAL IMPROVEMENT

Per Cent Decrease of Pressure	No. of Cases	Reduction in Classification			
		0	1	2	3
<10	5	1	4		
10 - 20	5	2	3		
21 - 40	2		1	1	
41 - 60	3		3		
61 - 80	2			1	1
Increased Pressure	1		1		

The patients were grouped for comparison on the basis of preoperative right ventricular pressure into Groups I, II, III, and A. Group I (seven patients) had preoperative systolic pressures between 30 and 45 mm. mercury. Group II (14 patients) measured between 46 and 80 mm., and Group III (nine patients), over 80 mm. The two in Group A did not have preoperative catheterization studies. The results are shown in Table I. In Group I three showed no functional improvement, while the other four advanced one class in functional capacity. Twelve in Group II advanced one class, and one patient improved two classes. In Group III seven patients advanced one class, one patient advanced two classes and another showed the maximum improvement of three classes. One from Group A advanced three classes and the other showed no improvement. Twelve had been unable to accept any employment or perform light household tasks. In 11 of these, improvement was sufficient to handle full-time employment at least of a sedentary type.

Other Symptoms

In evaluating symptoms not always associated with everyday function it was found that 13 patients had experienced episodes of hemoptysis at some time prior to their operations. During the entire postoperative period only five of these patients had experienced hemoptysis and two of these reported a marked decrease in the frequency of this symptom. There was no instance of hemoptysis appearing for the first time after surgery. The number of patients experiencing paroxysmal tachycardia was reduced from 13 to four. One patient noted this symptom for the first time subsequent to his operation.

Embolic Phenomena

Among the patients in this series prior to surgery there had been 27 definite episodes of peripheral embolization in 10—nine of these patients had auricular fibrillation. An additional two had probable emboli. In the interval between surgery and follow-up evaluation (which represented

700 patient months) there were no detectable episodes of peripheral embolization.

Murmurs

Careful auscultation permitted the detection of the diastolic rumble of mitral stenosis in every patient at the time of follow-up examination. In about one-third of the cases there was a marked decrease in the intensity of the murmur. This decrease did not consistently correlate with large decrease in right ventricular pressure or the absence of calcification of the valve.

Twelve patients were noted to have systolic murmurs at the apex before surgery and all 12 retained a murmur of approximately the same intensity

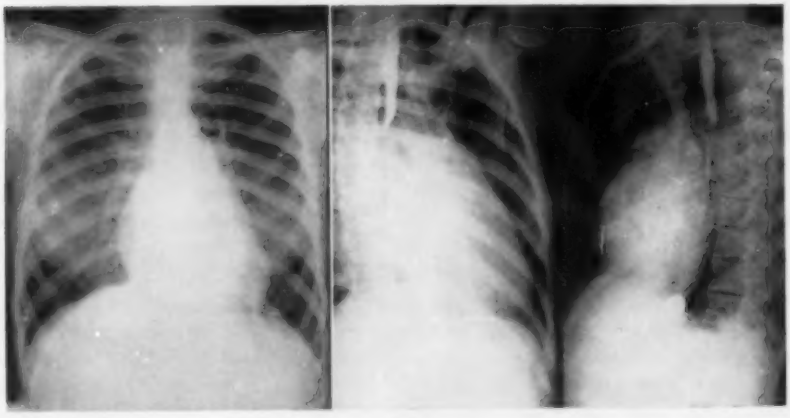

FIGURE 2A

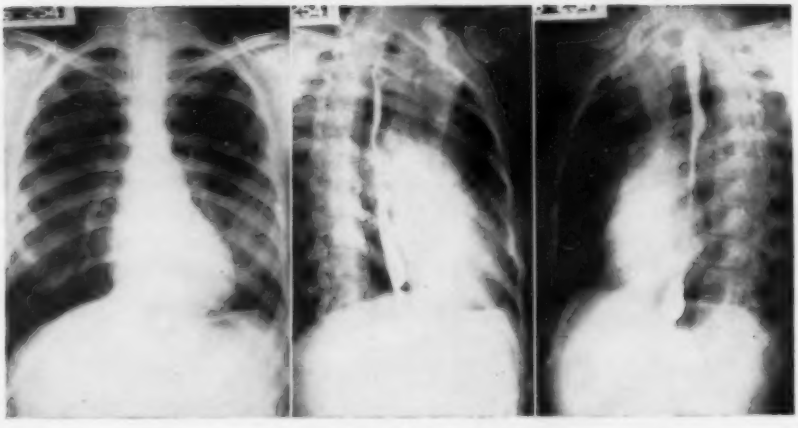

FIGURE 2B

Figure 2: (a) Preoperative chest x-ray films. (b) One year postoperative x-rays of the same patient. The patient showed an exceptional degree of change in cardiac size.

TABLE IV
ELECTROCARDIOGRAPHIC CHANGES

Group	Cases	Preop. Evidence of R.V.H.			No. R.V.H.		All Cases
		Cases with R.V.H.	Reversal of R/S in V1	Decr. R/S in V1	Decr. RV1 + SV5	Incr. RV1 + SV5	Incr. RV5 + SV1
I	7	0			2		1
II	14	8	2	4	2	1	8
III	8	7	6	1	1		6
A	1	1		1			

upon re-examination. In two of these cases the surgeon felt that there had been a decrease in the regurgitant jet following commissurotomy. Five were found to have systolic murmurs on follow-up examination who had not had this murmur before surgery. The surgeon had reported no regurgitation after commissurotomy in three of these and in a fourth equal slight regurgitation before and after the procedure.

Eight patients were noted to have an early diastolic murmur at the cardiac base prior to surgery. This was interpreted as due to relative pulmonic insufficiency although two of these patients had right ventricular pressures below 45 mm. On re-examination only two continued to have this murmur. One was in the low pressure group. In the other the preoperative right ventricular pressure was 109 mm. and the postoperative pressure 80 mm.

Right Ventricular Pressure Changes

Comparison of preoperative right ventricular pressure with the pressure at the time of follow-up recatheterization is tabulated as per cent of reduction of the preoperative value (Table II). In Group I (preoperative pressure 30-45 mm.) there was little possibility for change since the preoperative values were nearly normal. Two of the five restudied in this group showed less than 10 per cent decrease while two others showed 10 to 20 per cent decrease and one had a decrease of 40 per cent. Seven were restudied from Group II (preoperative pressure 46-80). Three had less than 10 per cent reduction in pressure; two had 10-20 per cent reduction; and one each showed 20-40 per cent decrease and 40-60 per cent decrease. One in this group showed a 25 per cent increase in pressure. The five in Group III (preoperative pressure above 80 mm.) all showed definite reduction in pressure. In one case this amounted to 20-40 per cent; in three cases, 40-60 per cent; and in the fifth case, 60-80 per cent.

Comparison of the decrease in right ventricular pressure with the improvement in functional capacity (Table III) indicates that there is only a rough relationship. The two cases with the greatest reduction in pressure did have marked to maximal functional recovery. The one case that showed an increase in right ventricular pressure when recatheterized was evaluated as showing an improvement of one grade in functional capacity.

TABLE V
PRESSURE CHANGES vs ELECTROCARDIOGRAPH

Per Cent Decrease of Pressure	Cases	Preop. Evidence of R.V.H.			No R.V.H.
		Cases with R.V.H.	Reversal of R/S in V1	Decr. R/S in V1	Decr. RV1 + SV5
<10	4	3		1	
10 - 20	4	1	1		2
21 - 40	3	1	1		1
41 - 60	2	1		1	
61 - 80	2	2	2		
Pressure Increase	1				

Electrocardiographic Changes

In 28 patients we were able to compare electrocardiograms at the time of follow-up examination with preoperative tracings (Table IV). The proportion of patients showing electrocardiographic evidence of right ventricular hypertrophy was greater with increased preoperative right ventricular pressure and the highest pressure group contained the greatest proportion of patients whose electrocardiograms showed a decrease of the R/S ratio in V1 from greater than one before surgery to less than one after surgery. In the entire series there were 16 who showed evidence of right ventricular hypertrophy before surgery. Half of these no longer had evidence of such hypertrophy in their follow-up electrocardiograms and six more showed definite decrease in degree of hypertrophy as measured by the R/S ratio in V1. Figure 1 illustrates the degree of change in electrocardiogram that was found.

Pre- and postoperative comparison was made of the sum of the millimeter height of R and V1 plus millimeter of depth of S in V5. It was felt that this may be an approximation of the relative vector force of the right ventricle. It was found that five who preoperatively had not met the criteria for right ventricular hypertrophy, nevertheless, did show evidence of decrease in the value of R V1 plus S V5 postoperatively while one patient showed increase in this value.

In the same manner R V5 plus S V1 was measured as an evaluation of the relative left ventricular vector force. Nine showed electrocardiographic evidence of increased R V5 plus S V1 after surgery. One had developed systemic hypertension. This group contained six of the nine patients in whom the surgeon had reported either a postcommissurotomy increase in the pre-existing regurgitant jet or the production of such a jet when it had not been present before the valve was manipulated. None of these patients showed enough increase in left ventricular preponderance to meet the criteria for left ventricular hypertrophy.

In Table V the electrocardiographic changes are compared with the decrease of right ventricular pressure. It can be seen that there is a rough relationship between these two measurements.

X-Ray

In 23 patients it was possible to compare preoperative chest x-ray films with follow-up films. Most of these comparisons revealed little change except for the loss of the left auricular appendage on the P.A. view. The transverse diameter decreased 16 per cent in one (Figure 2) and increased 20 per cent in another case. The latter had been hospitalized three times following surgery for reactivation of rheumatic fever. In the remaining cases there was less than 10 per cent change in the transverse diameter.

In seven cases there was a definite decrease in the width of the pulmonary artery. Five of these had been recatheterized and all had a decrease of at least 20 per cent in right ventricular pressure. Two others who had greater than 20 per cent decrease in right ventricular pressure did not exhibit demonstrable decrease in the pulmonary artery shadow. In three there was an increase in the pulmonary artery size. One of these had been recatheterized and showed no significant change in right ventricular pressure.

Operative Findings and Techniques

Among the cases in which the operative note included a statement regarding calcification of the valve there were 14 who did have calcification and 12 in whom this condition was not found. There was no consistent relationship between the presence or absence of calcification and clinical or laboratory results. The cases with calcification did not show an increased tendency to develop systolic apical murmurs or greater frequency of increased left ventricular force on the electrocardiogram. The surgeons did not report more cases of regurgitant jet after commissurotomy among those with calcified valves. Ellis et al[3] have reported 43 per cent failure in improvement after surgery in patients with scarred, immobile valves which were often calcified.

In nine cases both commissures were divided completely. In three the commissures were only partly cut because of the fear of producing too much regurgitation. In 14 cases only the anterior commissure was opened. The occurrence of maximum or minimum improvement did not depend on whether one or two commissures were opened. In four who had only anterior commissurotomy or only partial opening of the valve some of the initial evidence of improvement had receded by the time of final evaluation. This was due to reactivation of rheumatic fever in one case and the occurrence of myocardial infarction in a second. A markedly deformed and scarred valve had been found in a third case.

Pathological Findings

Pathological report of the left auricular appendage was available in sixteen patients in this series. In eight Aschoff bodies were present and

the interpretation was active rheumatic fever. There was no increased incidence of postoperative complications in this group and some of the best results were found among these cases. Similar results have been noted in other reports.[2, 3]

Lung biopsies were studied in 10 of our patients. In eight of these the report indicated chronic passive congestion with fibrosis. Unfortunately, none of these patients were recatheterized after surgery. Functional improvement was one grade in six of these and nil in the other two.

Postoperative Complications

There were no instances of emboli at surgery or during the convalescent period.

Two developed atelectasis and one had concomitant pericarditis. Two others developed pulmonary emboli although one of the episodes occurred one month after surgery.

Two had postoperative edema of the larynx, one of whom required a tracheotomy. In both cases there was good recovery.

One in this series and another who is not included in the series developed acute schizophrenic reactions during the first five days after surgery. Both cases required transfer to a mental hospital. One made a good recovery after electric shock therapy. The other could not be traced.

Nineteen had sinus rhythm before surgery. Two had previously been converted from auricular fibrillation. Both had recurrence of fibrillation after surgery, one on the second postoperative day and the other 15 months after surgery. Both were easily reconverted with quinidine. Two others fibrillated for the first time after surgery and also responded readily to quinidine therapy.

Five had strongly suggestive or proved episodes of recurrence of active rheumatic fever during the follow-up period. Some of these instances may have represented the so-called postcommissurotomy syndrome although only one case seemed to be typical of this. Three of these patients recovered without substantial loss of their improvement from surgery. One, aged 50, who had shown a moderate degree of improvement lapsed into about the same functional capacity as before surgery. This patient had had a deformed valve and only a partial commissurotomy had been possible. The fifth had three episodes of recurring rheumatic activity. The transverse diameter of his heart increased 20 per cent during this period. However, he eventually recovered to the point of being able to tolerate somewhat more activity than before surgery.

Discussion

The one to three year follow-up period in this series is still a relatively short time compared with the average natural duration of mitral stenosis. However, the finding that almost all the patients continued to maintain their postoperative improvement during this period is most encouraging and highly suggestive that the mechanical advantage of the divided commissures will be of continuing benefit to these patients. Since the im-

provement found in this series is similar to that reported in series with shorter follow-up periods it tends to substantiate the belief that the improvement is real and not merely due to postoperative rest or psychological factors. (Nevertheless, there is no doubt that these factors are operative in any subjective evaluation). The sustained improvement is even more impressive when one realizes that in many cases the immediate indication for surgery was progressive deterioration of functional capacity.

An evaluation of functional improvement is most accurately made by careful and intelligent evaluation of the patient's history.[4] Supposedly objective measurements such as graded exercise on a treadmill can be readily influenced by the subjective state of the patient or by physical fitness factors not directly related to the changes due to surgery. Since the subjective element cannot be eliminated any quantitation must be very approximate. Another group of investigators by the addition of just a little more enthusiasm or optimism could honestly find two grades of improvement in many of the patients whom we classified as showing only one grade improvement.

Ellis et al.[5] using a similar comparison of function in a group of 94 patients studied three months to three years following commissurotomy, found excellent results in 62 per cent and significant improvement in 24 per cent. Glover[6] reported that in one to five year follow-up in 319 cases 50 per cent had excellent results and 30 per cent were definitely improved. Ellis and Harkin[7] in reviewing 500 patients by examination or questionnaire reports six months to five years after surgery found significant improvement in 77 per cent. These findings are quite similar to the findings in the present study in which 85 per cent of the patients have shown at least one full grade of improvement. The results in these series are consistent with the general range of improvement reported in earlier series with shorter periods of follow-up. This strengthens the feeling that a permanent physiological improvement often results from this operation and discounts the importance of psychological factors and postoperative rest.

The definite curtailment of the symptoms of hemoptysis and paroxysmal nocturnal dyspnea is concrete evidence of improved physiological status.

The electrocardiographic changes reported confirm previous findings:[8] that in mitral stenosis only the higher levels of right ventricular hypertension are likely to be reflected in the electrocardiograph pattern of right ventricular hypertrophy. In addition, we now find that this pattern is often reversible when the hypertension is lowered. This strongly suggests that the term "right ventricular hypertrophy" which assumes an anatomical change is a misnomer. The electrocardiogram reflects a dynamic physiological state of increased pressure or load rather than the more static hypertrophy which often is a concomitant of this state. The older term, of "right ventricular strain" seems more descriptive. Other postcommissurotomy studies[9, 10] have also reported reversibility of the strain pattern in a significant proportion of cases. We agree with these authors that when the pattern of right ventricular hypertrophy is present in a case of mitral stenosis, careful observations of changes in this pattern is

an excellent index of dynamics in the pulmonary circulation and correlates with clinical improvement.

Sustained reversal of physiological pathology as demonstrated by right ventricular pressure and electrocardiographic changes is evidence of the persistent effectiveness of the surgical correction. It is encouraging that some advanced cases with marked elevation of right ventricular pressure and electrocardiographic evidence of hypertrophy are capable of reverting to normal in respect to these measurements.

One of the most encouraging findings is the effectiveness of left auricular appendectomy with commissurotomy in sharply reducing the incidence of peripheral emboli even with persistence of auricular fibrillation. Ellis and Harken[7] were also impressed by the protection from the danger of late embolization. In their group of 440 surviving patients who had been followed for an average of 22 months only five had late peripheral embolization although more than half were fibrillating. However, among the 71 patients in their series who had preoperative episodes of embolization and were fibrillating at the time of surgery 17 developed emboli at the time of surgery.

CONCLUSION

The large majority of carefully selected cases of mitral stenosis with functional impairment submitted to commissurotomy benefit from the procedure and in many cases this benefit persists for at least one to three years.

A greater degree of benefit can be anticipated in otherwise satisfactory cases when the right ventricular pressure is markedly elevated. Such elevation can usually be predicted when evidence of right ventricular strain is present on the electrocardiogram.

In addition to evidence of improvement in respect to functional capacity, hemoptysis, and paroxysmal dyspnea, a large proportion of cases had objectively demonstrable improvement. This is evident in reduction of right ventricular pressure and decrease of right ventricular force on the electrocardiogram. Decrease in heart size by x-ray is an exceptional finding.

Mitral commissurotomy with auricular appendectomy is an effective method for controlling peripheral emboli in patients with mitral stenosis.

The presence of a calcified valve may not necessarily prevent lasting or significant benefit from the procedure.

CONCLUSION

La mayoría de los casos cuidadosamente seleccionados de estenosis mitral con trastorno funcional que se han sometido a comisurotomía se benefician por el procedimiento y en estos casos este beneficio persiste por lo menos de uno a tres años.

Mayor grado de eficacia puede preverse en casos que por otra parte son satisfactorios cuando la presión ventricular derecha es marcadamente elevada. Tal elevación puede habitualmente predecirse cuando hay evidencia de sobrecarga ventricular derecha en el electrocardiograma.

Además de la evidencia de mejoría respecto de la capacidad funcional,

hemoptisis, disnea paroxística, una proporción grande de casos tenía evidencia objetiva. Así lo muestra la reducción de la presión ventricular derecha y el decrecimiento de la fuerza ventricular derecha según el electrocardiograma.

El decrecimiento del tamaño del corazón a los Rayos X es excepcional.

La comisurotomía mitral con apendectomía auricular es un método efectivo para controlar los émbolos peri-féricos en los enfermos de estenosis mitral.

La presencia de válvula calcificada no implica necesariamente una falta de beneficio significativo duradero después de este procedimiento.

RESUME

La grande majorité des cas soigneusement choisis de sténose mitrale, avec troubles fonctionnels, soumis à la commissurotomie retirent un bénéfice du procédé et dans beaucoup de cas cette amélioration persiste pendant au moins 1 à 3 ans.

On peut prévoir une amélioration plus importante pour des cas par ailleurs satisfaisants, lorsque la pression du ventricule droit est élevée d'une façon nette. Une telle élévation peut habituellement être prévue lorsque l'électrocardiogramme met en évidence une fatigue du ventricule droit.

Outre la mise en évidence d'une amélioration en ce qui concerne la capacité fonctionnelle, les hémoptysies et la dyspnée paroxystique, un grand nombre de cas eurent une amélioration objectivement constatable. La réalité apparait évidente par la réduction de la pression ventriculaire droite et la diminution de la puissance ventriculaire droite sur l'électrocardiogramme. Une diminution du volume du coeur est une constatation radiologique exceptionnelle.

La commissurotomie mitrale est un procédé efficace pour juguler les embolies périphériques chez les malades atteints de sténose mitrale.

La présence d'une valvule calcifiée n'est pas forcément un obstacle soit à la qualité, soit à la durée de l'action favorable de la méthode.

SCHLUSSFOLGERUNG

Die überwiegende Mehrzahl sorgfältig ausgesuchter Fälle von Mitralstenose mit Funktions-Einschränkung, bei denen eine Kommissurotomie durchgeführt wurde, wird durch diese Operation gebessert. In vielen Fällen hält die Besserung mindestens 1-3 Jahre an.

Die Besserung wird dann um so grösser sein, bie dem Patienten ein guter Allgemeinzustand vorliegt, aber der Druck im rechten Ventrikel deutlich erhöht ist. Diese Erhöhung kann im allgemeinen vorausgesagt werden, wenn aus dem Elektrokardiogramm eine Überlastung des rechten Ventrikels zu ersehen ist.

Aus der Besserung hinsichtlich der Belastungsfähigkeit, der Hämoptysen und der paroxysmalen Dyspnoe ist bei einer grossen Zahl von Patienten eine Besserung objektiv nachweisbar. Diese tritt in einer Verminderung des Druckes im rechten Ventrikel hervor sowie in einer Rückbildung der elektrokardiographischen Zeichen der Rechtsüberlastung.

Eine Abnahme der röntgenologisch messbaren Herzgrösse ist ein ausnahmsweiser Befund.

Mitral - Kommissurotomie mit Herzohrresektion ist eine wirksame Methode zur Verhütung der Embolisierung bei Patienten mit Mitralstenose.

Das Vorhandensein einer verkalkten Klappe schliesst nicht notwendigerweise eine dauerhafte oder bedeutende Besserung durch die Operation aus.

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The Half-Second Expiratory Capacity Test: A Convenient Means of Evaluating the Nature and Extent of Pulmonary Ventilatory Insufficiency

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Pulmonary ventilatory insufficiency is a manifestation of many clinical disorders both pulmonary and non-pulmonary by primary nature. Regardless of the origin of ventilatory dysfunction, it may be classified as one of three types: 1) restrictive, that is with a decrease of pulmonary stroke volume; 2) obstructive, that is impaired pulmonary air flow; or 3) combined, that is both obstructive and restrictive ventilatory insufficiency.

An appreciation of the nature and extent of ventilatory insufficiency in any given clinical situation is important not only for the purpose of the elucidation of altered basic physiological mechanisms, but also for the value that such knowledge imparts toward the proper selection and evaluation of treatment. Thus the development of a precise and yet convenient method for evaluating ventilatory defects is indicated. The purpose of this report is to illustrate the use of such a method which was described elsewhere by us.[1, 2, 3]

To properly describe ventilatory insufficiency a test must evaluate both pulmonary stroke volume and the velocity of air flow. Matheson and associates[4] suggested the capacity ratio $\left\{\frac{\text{MBC-L/min}}{\text{VC-L}}\right\}$ while Gaensler[5] introduced the air velocity index $\left\{\frac{\text{MBC\% Pred.}}{\text{VC\% Pred.}}\right\}$ We have not found either of these tests satisfactory as a means of differentiating the types of ventilatory insufficiency.[2, 3] The principal shortcoming appears to arise from the variability intrinsic in the MBC. More recently Gaensler[6] has suggested measurement of the first one second portion of the vital capacity as an estimate of the MBC and the ratio of the one second expiratory capacity (1.0 sec. EC) to the total vital capacity (TVC) as a means of identifying obstructive ventilatory defects. He found the 1.0 second capacity to average 83 per cent of the vital capacity in 35 normal subjects. Kennedy[7] has indicated that the first 0.75 second portion of the TVC represents that segment of the expiratory flow curve utilized in performing the MBC, and further that the 0.75 second volume could be used for the indirect determination of a function which is comparable to the MBC but which Kennedy identified as the ½ maximum flow rate. Kennedy suggested that the first 0.75 second rapid expiratory volume is delivered essentially at a constant maximum rate of flow. After 0.75 seconds he

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TABLE I
EFFECT OF NON-PULMONARY FACTORS ON MBC AND 0.5 SEC. EC X 60

	0.5 Sec. EC*	MBC*	Predicted MBC*
1. 26 yr. WM 3 mo. bed rest	168	110	175
2. 29 yr. WF 2 mo. bed rest	132	90	130
3. 50 yr. WM 25 lb. Wt. loss	138	85	145
4. 42 yr. WM Mentally disturbed	144	80	160

*All Values Liters per Minute.

found that flow abruptly decreases resulting in a break in the volume curve. These conclusions were criticized by Bernstein[8] who found the rapid expiratory curve was a smooth curve without a straight portion or a critical point of inflexion. He also presented evidence to indicate that the characteristics of the rapid expiratory flow curve described by Kennedy were artefactual and could be attributed to impaired frequency response characteristics of the recording apparatus used by Kennedy.

In order to investigate methods of conveniently obtaining information concerning the nature and extent of ventilatory insufficiency, vital capacity measurements were made with a Gaensler-Collins Timed Vitalometer modified by us so that it was possible to measure accurately the first 0.5, 0.75 and 1.0 second segment of the rapid expiratory volume. In the light of the work of Bernstein it became necessary to evaluate the characteristics of the rapid expiratory flow curve obtained by this method. Using a high speed low torque potentiometric recorder described previously[2] smooth rapid expiratory flow curves of the type described by Bernstein were obtained. The 0.5 second volumes were virtually identical as obtained by both of the above methods. This method was further subjected to a comparison with the integral volume curve obtained from a pneumotachographic flow tracing, and again smooth curves virtually identical with the recorded curves were obtained. Figure 1 is an example of a rapid expiratory curve obtained by integration of a pneumotachographic tracing. D'Siland and Kazantis[9] in studies reported subsequent to the completion of this work found that the actual rapid expiratory flow curve was very similar to an exponential curve but deviates from an ideal curve at a point in time very close to 0.5 second (0.47 $\pm$ 0.09 second). It was found by us also, in previous studies[1, 2, 3] that the 0.5 second expiratory capacity (0.5 sec. EC) is the most satisfactory estimate of the maximum velocity of expiratory air flow. Analysis of the first portion of a characteristic normal rapid expiratory flow curve (Figure 1) reveals that the first 0.5 second portion of the vital capacity virtually represents the segment of maximum air flow. (A line OA with its origin at zero time and tangent to the rapid expiratory flow curve would represent an average of the maximum flow rate for the period of time utilized for expiration). Thus in a

single test both 0.5 sec. EC, a measure of the rapidity with which an individual can ventilate his lungs, (referred to here as velocity of air flow), and the TVC, a measure of the maximum pulmonary stroke volume are obtained.

Since the MBC in individuals with normal pulmonary air flow is an estimate of the ½ maximum flow rate, it might be expected that an MBC in turn might be estimated by expressing the rapid portion of the expiratory curve as liters per minute. Assuming expiration and inspiration to be approximately equal in time during rapid breathing, and estimated MBC would be obtained as shown by the formulation in Figure 1, where $MBC_{est.}$ = 0.5 sec. EC x 60. In previous studies[2] the 0.5 sec. EC x 60, in normal subjects, was shown to correlate better with the actual measured MBC than do $MBC_{est.}$ values derived from other timed expiratory capacities. The relationships between diagrammatic representations of various characteristic rapid expiratory flow curves and the 0.5, 0.75 and 1.0 second intervals utilized in these tests are shown in Figure 2 with the maximum breathing tidal volumes from a normal subject and two patients; one with an obstructive ventilatory defect and another with a restrictive ventilatory defect. Particularly apparent is the fact that the patient with obstructive breathing cannot represent his average maximum velocity of air flow with

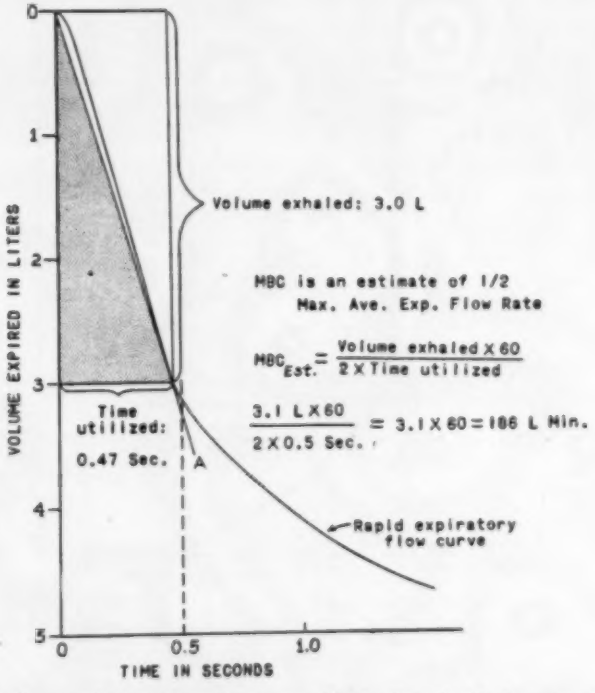

FIGURE 1: A normal expiratory flow curve illustrating the basis upon which an estimate of average maximum minute ventilatory capacity can be made.

an MBC effort, since in order to maintain a satisfactory degree of alveolar ventilation, he must utilize a relatively large tidal volume and a slow rate over a portion of his expiratory curve where air flow is slow. This figure further serves to illustrate certain variables that would affect the value of the actual MBC. It is known that the results of the MBC test are dependent to a large extent on neuromuscular coordination, cooperation, muscular strength and durability, but it now becomes apparent that the tidal volume, the breathing rate, and the segment of the expiratory flow curve utilized to perform the test are equally as important determinants. These are all factors which are to a large extent under voluntary control. This point receives additional emphasis from the values shown in Table I. These data show that in individuals with normal respiratory function, abnormal MBC's may be obtained owing to non-pulmonary factors whereas the 0.5 sec. EC x 60 provides a more reliable estimate. Thus it can be

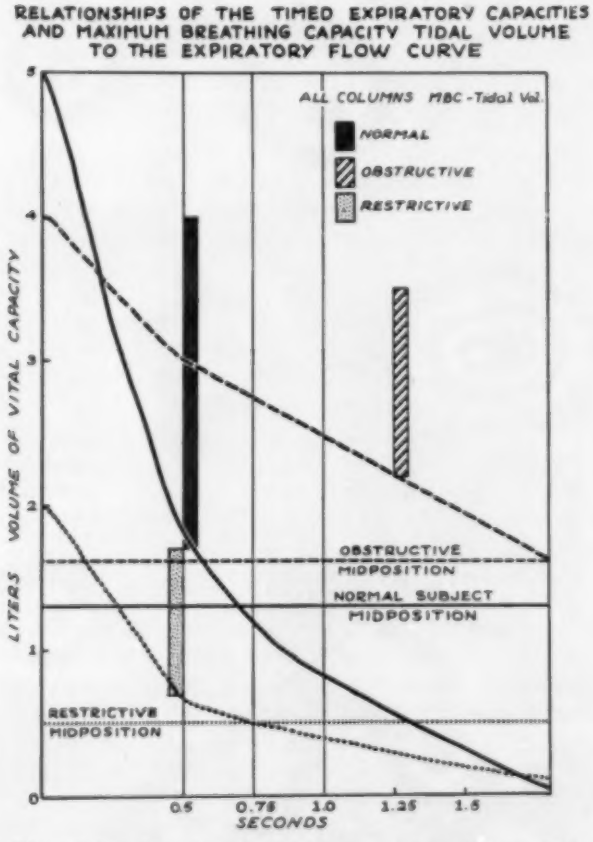

FIGURE 2: The relationships between three types of expiratory flow curves with respect to the 0.5, 0.75, and 1.0 second time interval and the respective maximum breathing tidal volumes.

shown that the MBC is to a large extent a performance test and that maximum ventilatory capacity could be more precisely determined from the rapid segment of the rapid expiratory volume curve (i.e., the 0.5 sec. EC x 60).

In order to obtain a method whereby one can characterize the velocity of air flow for purposes of comparing different individuals, and thus have a test for defining the nature of altered lung function, we related the 0.5 sec. EC to the TVC so as to obtain a ratio, $\frac{0.5 \text{ sec. EC} \times 100}{\text{TVC}}$. The validity of this relationship was tested previously[2] where it was also shown that this ratio was the most convenient for separating various ventilatory defects. There is no age or sex regression of the $\frac{0.5 \text{ sec. EC} \times 100}{\text{TVC}}$ ratio whereas there is with the other timed expiratory capacity ratios, as well as the air velocity index and the capacity ratio. Moreover less overlapping of results between individuals with apparent normal and abnormal states of air flow was noted with the 0.5 sec. ratio as compared to other tests.

We have shown that the normal value for the ratio $\frac{0.5 \text{ sec. EC} \times 100}{\text{TVC}}$ should be more than 60 per cent and the TVC should normally be more than 80 per cent of the predicted normal.[2] By the use of these functions and their normal limit values as determinants in a quadrant system, illustrated in Figures 3, 4, 5, and detailed elsewhere,[3] a simple method is obtained for the separation of ventilatory defects into three categories: restrictive, obstructive, and combined obstructive-restrictive. In each of Figures 3, 4, and 5 are presented several examples of cases studied by this

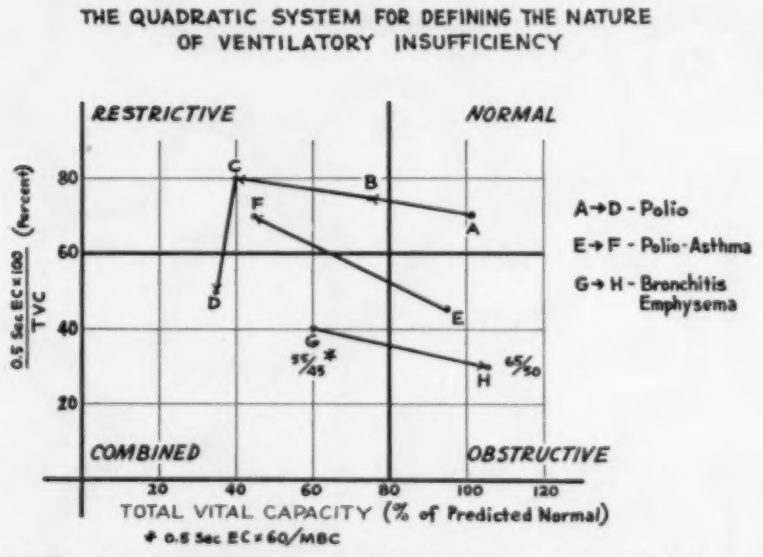

FIGURE 3: The quadrant system utilized for the evaluation of serial studies on patients with various ventilatory disorders. See text for detailed description.

method to demonstrate the nature of the changes in ventilatory function during the course of the disease or under the impact of therapy. Each capital letter represents the result of a test. Where numerical values are shown, they are the 0.5 sec. EC x 60 and the MBC.

In Figure 3, ABCD represents data obtained from a 16 year old white male with poliomyelitis who developed progressive diaphragmatic and intercostal muscular paresis which resulted in a restrictive ventilatory disorder as shown A to C. Even though the TVC decreased, the ratio showed a tendency to increase indicating the loss of volume consisted predominantly of slow moving air. This provides a very sensitive and important test for poliomyelitis patients as is apparent at C-D which illustrates the development of an obstructive component due to pooling of secretions and relaxation of the intrinsic muscles of the larynx. Tracheotomy was definitely indicated at this point.

Case E-F is an interesting and unusual example of poliomyelitis developing in a 29 year old white male known asthmatic who had no recognizable respiratory symptoms at E. The obstructive defect could be promptly relieved by bronchodilator nebulization which was continued, but the patient developed some respiratory muscle weakness and a superimposed restrictive ventilatory disorder became apparent.

An example of precisely the opposite effect is case G-H which represents data from a patient with bronchitis and emphysema who when first studied had a restrictive and obstructive or combined type ventilatory disorder. After antibiotics and nebulization treatments with a bronchodilator drug and a surface active wetting agent which resulted in the

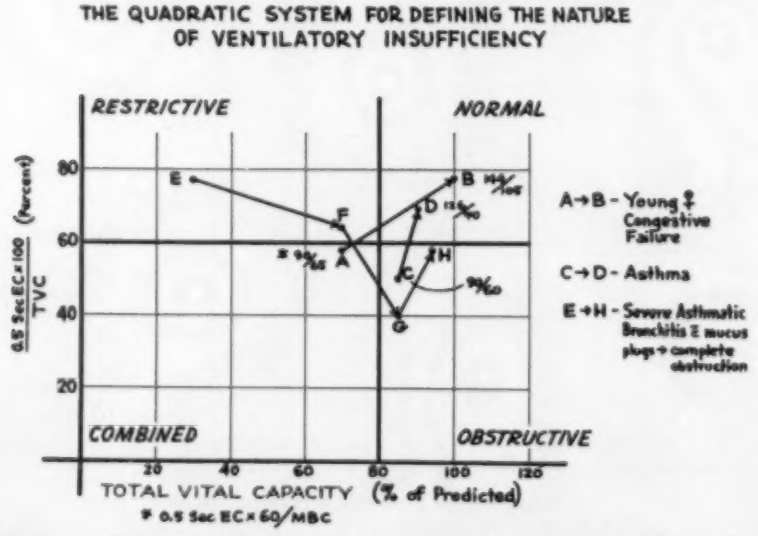

FIGURE 4: The quadrant system utilized for the evaluation of serial studies on patients with various ventilatory disorders. See text for detailed description.

evacuation of much mucopurulent sputum with mucus plugs, the TVC increased but the $\frac{0.5 \text{ sec. EC} \times 100}{\text{TVC}}$ ratio decreased indicating that the volume added was predominantly slow moving air, probably from emphysematous lung.

In Figure 4, A-B represents data from a young patient with recent congestive failure before (A) and after (B) compensation. At A, even though he had a predominantly restrictive ventilatory defect, the "obstructive" component became apparent by the change after compensation at B, since an increase in the velocity of air flow as well as the maximum pulmonary stroke volume resulted. Patients with early congestive failure without bronchopulmonary disease usually reveal predominantly a restrictive defect, whereas patients with chronic congestive failure or congestive failure and bronchopulmonary disease exhibit a combined disorder.

Patient C-D in Figure 4 is an example of values obtained from a young asthmatic patient before and after a treatment with nebulized bronchodilator. The change has been predominantly an increase in the velocity of air flow as indicated by the rising ratio.

The data shown at E-H in Figure 4 represent the results of an interesting and unusual situation observed in a young woman with severe asthmatic bronchitis and emphysema. Point E which was obtained soon after admission indicates that the ventilatory defect was restrictive in nature even though the patient is known to have anatomically obstructive disease. This apparent paradox is interpreted to mean that a large segment of the slow-moving air has been lost, most likely as a result of multiple bronchial

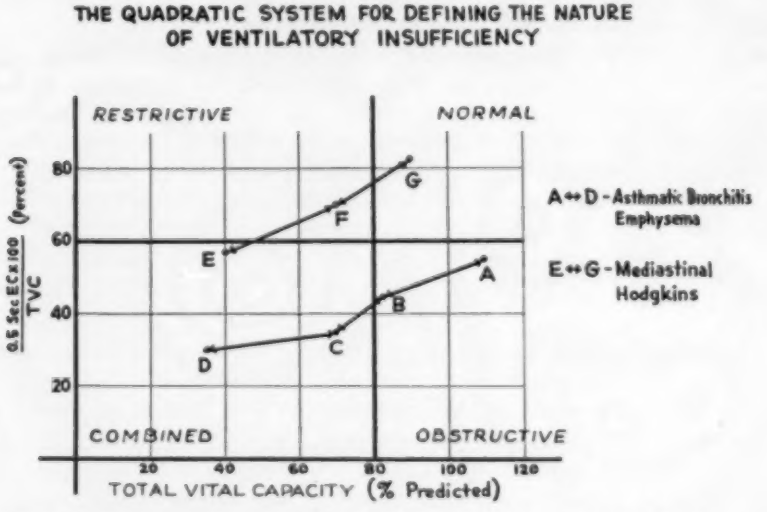

FIGURE 5: The quadrant system utilized for the evaluation of serial studies on patients with various ventilatory disorders. See text for detailed description.

plugs associated with the patient's acute infection. After treatment with bronchodilator, surface active wetting agent, and Pancreatic Dornase R* nebulization, the vital capacity increased as shown at Point F, but the ratio $\frac{0.5 \text{ sec. EC} \times 100}{\text{TVC}}$ decreased indicating that the added volume was predominantly slow moving air. At point G there was again slightly greater improvement of the total vital capacity with a further decrease of the 0.5 sec. ratio, perhaps in part due to the addition of more slow moving air to the total displaceable lung volume, and perhaps in part a result of some superimposed incomplete bronchial obstruction. The patient's function studies at the time of discharge were shown at Point H indicating a further increase in the TVC, but now a striking increase in the velocity of air flow suggesting further that the marked decrease at Point G was due to either bronchospasm or other type of incomplete bronchial obstruction.

Figure 5 represents the results obtained from two patients who were studied many times and were found to move back and forth across the quadrant graph as indicated by the bi-directional arrows. In each instance here, a point usually represents the average of several studies. The first patient, A-D, with severe recurrent asthmatic bronchitis has been noted to follow the pathway A to B to C to D during the course of the development of an exacerbation and to virtually reverse this pathway from D to A during recovery. During the development of an exacerbation with the accumulation of obstructing secretions and bronchospasm, he developed a combined; obstructive-restrictive; ventilatory defect (D). Upon recovery, increases of both the TVC as well as the net velocity air flow, as indicated by a rising ratio from D to A, were noted. This patient was ultimately left with an obstructive ventilatory defect (A) either due to a permanent degree of bronchiole obstruction or pulmonary emphysema.

Patient E-G is a young man with mediastinal Hodgkin's disease who, when first seen at Point E, had large obstructing and restricting mediastinal nodes. Following treatment, he improved progressively with the resolution of the mediastinal nodes through Point F to Point G where he was found to have essentially normal pulmonary ventilatory function. With exacerbations of his condition or the development of intercurrent infection, change in his ventilatory function was characterized principally by a decrease in pulmonary stroke volume, but ultimately he returned to a point in the vicinity of E with a combined obstructive and restrictive ventilatory defect.

Thus these serially studied cases illustrate the valuable and yet conveniently obtained information concerning the nature of the ventilatory defects that becomes available by the use of this method of functional analysis.

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*Pancreatic Dornase R, desoxyribonuclease extracted from beef pancreas, is a very effective mucolytic enzyme which appears to be free of the undesirable features of other enzymes used for this purpose. This drug was kindly supplied by Sharp & Dohme, Division of Merck & Co., Inc., Westpoint, Pa.

ADDENDUM

Additional data that has become available since the submission of this paper makes it necessary in the interests of uniformity to change the quadrant plot to the extent that the lower limit of the vital capacity should be placed at 85 per cent of predicted instead of 80 per cent as shown. We also feel now that the word "total" which precedes the term "vital capacity" in this manuscript is superfluous.

SUMMARY

A simple method employing single maximum expiratory efforts is presented as a means of defining the nature and extent of ventilatory insufficiency. The method involves the measurement of the 0.5 sec. expiratory capacity and the total vital capacity. Then by relating the 0.5 sec. expiratory capacity to the total vital capacity as a simple ratio, and expression of the maximum velocity of air flow during expiration, is obtained. The total vital capacity is a measure of maximum pulmonary stroke volume. Thus in a single test expressions of the velocity of pulmonary air flow as well as pulmonary stroke volume are found. If these functions are plotted against each other in a quadrant graphic system which is based on normal values for these two functions, a convenient and precise clinical method for defining the physiological nature of ventilatory insufficiency is obtained. This test is applicable even to the seriously debilitated patient who cannot perform the maximum breathing capacity test. Serial studies by this method provide a convenient and informative method of studying the nature of the change in ventilatory function during the course of the disease or resulting from therapy.

RESUMEN

Se presenta un método sencillo que emplea esfuerzos máximos únicos para determinar la naturaleza y grado de la insuficiencia ventilatoria. Los métodos comprenden la medida de la capacidad expiratoria en 0.5 segundos y además la capicadad vital total. Entonces estableciendo relación entre ambas medidas como dato único, se obtiene una expresión de la velocidad máxima de la corriente aérea expiratoria. La capacidad vital total es una medida del volumen pulmonar máximo en un solo esfuerzo. Así en una simple prueba se encuentran las expresiones de la velocidad de la corriente de aire expirado y la del volumen pulmonar de un solo esfuerzo. Si estas functiones son colocadas en contraposición en un sistema cuadrante gráfico que se base en los valores normales do estas dos funciones se logran un método clínico preciso para definir la naturaleza fisiológico de la insuficiencia ventilatoria. Esta prueba es aplicable aún a los enfermos muy seriamente debilitados que no pueden hacer la prueba de la capacidad respiratoria máxima. Los estudios en serie de este método proporcionan un método informativo en el curso de la enfermedad o para valuar resultados terapéuticos.

RESUME

L'auteur présente une méthode simple utilisant les seuls efforts d'expiration maximum pour déterminer la nature et le degré de l'insuffisance ventilatoire. Cette méthode comporte la mesure du volume expiratoire maximum en une demiseconde, et celle de la capacié vitale. En faisant le rapport du volume expiratoire maximum en une demi-seconde et de la

capacité vitale, on obtient une expression de la vitesse maximum du courant aérien pendant l'expiration. La capacité vitale est la mesure du plus grand volume de détente pulmonaire. On obtient ainsi en un seul test l'expression de la rapidité du courant aérien, et celle du volume ventilatoire. Si ces valeurs sont reportées sur un graphique gradué en fonution de leurs chiffres normaux, on obtient une méthode clinique précise pour déterminer la nature physiologique de l'insuffisance ventilatoire. Ce test est applicable même aux malades sérieusement atteints, qui ne peuvent pas effectuer une ventilation maximum. Des examens répétés par cette méthode permettent d'étudier la nature des variations de la fonction ventilatoire pendant l'évolution d'une maladie, ou à la suite d'un traitement.

ZUSAMMENFASSUNG

Zur Beurteilung von Art und Ausdehnung einer respiratorischen Insuffizienz wird eine einfache Methode, die sich eines einzelnen maximalen Exspirations-Stosses bedient, beschrieben. Die Methode erfordert die Bestimmung der Exspirations-Kapazität in einer halben Sekunde und der Vitalkapazität. Indem man die Halbsekunden-Exspirations-Kapazität zu der Vitalkapazität in Beziehung setzt, wird ein Ausdruck für die maximale Luftströmungsgeschwindigkeit während der Exspiration gewonnen. Die Vitalkapazität ist ein Mass des maximalen Atemvolumens; so kann mit einem einzelnen Test sowohl die Strömungsgeschwindigkeit der Luft als auch das nutzbare Lungen-volumen gemessen werden. Wenn diese beiden Funktionen auf einem Koordinatensystem eingetragen werden, das auf den Normalwerten basiert, wird eine leichte und genaue klinische Methode zur Bestimung der Art der ventilatorischen Insuffizienz gewonnen. Dieser Test kann sogar bei schwerkranken Patienten angewandt werden, bie denen kein Atemgrenzwert bestimmt werden kann. Serienuntersuchungen mit dieser Methode geben die Möglichkeit, die Art der Veränderungen der ventilatorischen Funktion im Verlaufe der Krankheit oder als Folge einer Behandlung zu studieren.

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Tuberculosis and Pregnancy

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How to advise and care for the woman handicapped by tuberculosis during her child-bearing years has for centuries perplexed the physician. Medical literature reflects differences of opinion so startling that some years ago Krause[1] summarized it as follows: "Whether the individual inquiry approaches the problem biologically, statistically or, say, physiologically, it is at once apparent that with few exceptions, the usual and average study proceeds from fallacious premises, gratuitous assumptions and almost complete lack of definite limitations of terms; and that from so unstable a foundation it limps through a morass of slipshod data and the crudest handling of evidence to a palpably questionable conclusion."

Tuberculosis has always been too unpredictable a disease to allow valid statistical study of its probable course and factors modifying the ultimate outcome.

From even a cursory review of the literature, it is evident that attitudes toward the problems of tuberculosis and pregnancy strongly reflect the social and economic influences of the period in which a given physician wrote. It is possible that many of the contrasting opinions arose largely because tuberculous patients were seen under so many varied circumstances that observers noted patients having little in common except tuberculous lesions and a gravid uterus. It is always to be emphasized that no two individuals react alike to infection with tubercle bacillus; it is also probable that no two women act alike during pregnancy or that no woman acts uniformly through multiple pregnancies. Recognizing that the interplay of only these factors will produce a number of clinical combinations, it is easy to understand that a clinical approach satisfactory for one woman might be wholly unsatisfactory for another woman whose clinical problem seemed superficially similar. Because of these considerations, little is to be achieved by a review of the world literature on the interactions of tuberculosis and pregnancy. The physician in practise can obtain little help in solving his clinical problems in this regard from a study of the literature reflecting conclusions drawn before specific chemotherapy for tuberculosis was available.

Because of the foregoing, it seemed advisable to study a series of tuberculous women whose obstetrical care was provided largely or in part at the Charity Hospital of Louisiana. Most of them were young colored women receiving antibiotic therapy in accordance with the prevailing therapeutic customs. Sixty-four cases were believed to be sufficiently informative for study; no attempt at selection was made. Although this series is small and has the defect of only short-term follow-up, it has the merit of personal acquaintance with the conditions under which these people were treated.

Presented at the Annual Meeting, Alabama Chapter, American College of Chest Physicians, Montgomery, April 20, 1955.

Another change in the times must be noted. Whereas formerly the weighty decisions concerning tuberculosis in pregnancy were made by the sanatorium physician, today these lie within the province of the practitioner. Quite frequently tuberculosis is brought to light only when the woman reports for supervision during pregnancy; this is especially true in patients who have returned to normal full activities after treatment for tuberculosis. The clinician must often advise whether pregnancy should be sanctioned, simply condoned or even forbidden. Opinions herein expressed are based on the experiences in the treatment of 64 women in poor social and economic circumstances. The majority were treated with varying combinations of streptomycin, para-amino-salicylic acid and isoniazid; a number had undergone collapse or excisional therapy. No attempt is made to reach statistical conclusions, but a sufficient number of impressive cases were seen to warrant certain clinical formulations.

I. Hazards in Tuberculosis to the Pregnant Woman

Physician and patient alike are frequently fearful that tuberculosis will become worse during the course of pregnancy. The aphorism of Young:[2] "If a virgin, no marriage; if married, no children; if pregnant, no delivery" —was formulated at a time when it was generally believed that pregnancy could not be tolerated by the tuberculous woman. So pessimistic an attitude is not justified either by recent authors or by the results of treatment in these 64 patients. While pregnancy does unquestionably impose a burden on the tuberculous woman, this burden is not insuperable. The risks while tuberculosis is active cause us to counsel deferment of pregnancy until the tuberculosis has reached the stage of inactivity (National Tuberculosis Association Diagnostic Standards 1950) for two years if minimal, three years if moderately advanced and five years if far advanced.

The familiar tragedy of rapidly progressing tuberculosis in the pregnant or parturient woman has left its impress on medical thinking.

Case 1: C. S. was a colored girl, 17 years old, when first observed as a tuberculosis contact in 1938. She was delivered of her first child October 10, 1940 and her second September 1, 1941. After pneumothorax was initiated October 11, 1942 she was admitted to Charity Hospital May 11, 1943 and remained there for only one month. She was readmitted with tuberculous laryngitis August 24, 1943, again deserting shortly after the delivery of her third baby October 11, 1943. She had no treatment at all and was finally admitted in a terminal state August 31, 1946.

Case 2: V. J. R. was a 22 year old colored female admitted during the sixth month of her fourth pregnancy May 27, 1952 because of chills, fever and a seven pound weight loss. She aborted a five and one-half month old fetus the next day and then had increasing pyrexia unaffected by the antibiotics administered; after the development of chest pains and jaundice, she was suspected of having septic phlebothrombosis; so ligation of the inferior vena cava was performed June 3, 1952. A few hours later rales were noted over both lungs, and her sputum was found to contain acid fast bacilli. She died that night; at autopsy, acute miliary tuberculosis with pulmonary infarction were detected. No calcified primary focus was found, but she had bilateral tuberculous salpingitis which presumably gave rise to decidual infection leading to spontaneous abortion, tuberculous septicemia and pulmonary infarction.

Current therapy of tuberculosis permits granting week-end passes and early return to outpatient status, two factors which operate against standardization of gestational time-tables. Many such pregnancies are carried through to full term delivery without detectable exacerbation or relapse of tuberculosis. Because of the multiplicity of factors which determine whether a tuberculous person will achieve permanent inactivation of

the disease or will succumb to its generalization, it is almost impossible statistically to demonstrate the influences of the pregnancy on the tuberculosis.

It is rather interesting to note that when tuberculosis has become inactivated, regardless of the methods of treatment used, it seems not to be reactivated by pregnancy. Many a patient has been safely carried through pregnancy while receiving pneumothorax; others following lobectomy, pneumonectomy or thoracoplasty, have not been disturbed by pregnancy.

Case 3: A. S. was 26 years old when her tuberculosis was discovered in 1944 after conclusion of her tenth pregnancy. The right lung was compressed by pneumothorax from 1944 thru 1949 at which time she was an outpatient and her tuberculosis regarded as inactive. Pregnancy number 11 ended in premature delivery June 21, 1949 but the baby survived. Pregnancy number 12, August 5, 1950, and number 13—August 13, 1951 terminated in normal full term deliveries. Her tuberculosis did not undergo reactivation.

Case 4: J. M. C. was 25 years old when her tuberculosis was found to be active June 13, 1946. Left pneumothorax was done April 23, 1946 to June 21, 1948. Right pneumothorax was done June 21, 1948 to August 7, 1948. A left thoracoplasty was done January 24, 1949. Her first pregnancy was terminated July 23, 1950 by Caesarean section using spinal anesthesia because of a low vital capacity. Her second pregnancy June 19, 1951 and her third pregnancy January 18, 1953 were spontaneous and uncomplicated.

Case 5: A. C. was diagnosed November 6, 1947 at the age of 26 years. She received antibiotics through 1948 and subsequently in 1951. Left phrenic crush in 1948 was only partially successful; it was necessary to do left pneumonectomy June 23, 1952. Subsequently she became pregnant twice and was delivered by Caesarean section December 4, 1953 and again February 8, 1955. Her most recent examination March 1, 1955 indicates that her tuberculosis is now inactive.

Case 6: A. A. was first found to have tuberculosis March 15, 1949 while 27 years old and in her third pregnancy which terminated September 4, 1949 with spontaneous full term delivery. Drugs started July 13, 1949 and continued through November 19, 1954 and again August 15, 1952 through February 25, 1953. Left upper lobe lobectomy was done October 8, 1949, a left phrenic the following month, pneumoperitoneum being continued until July 7, 1953. She was delivered of her fourth child November 5, 1951 spontaneously and was found to have inactive tuberculosis September 17, 1954.

That pregnancy probably does exert a deleterious effect on some tuberculous women is suggested by at least two factors: (1) the uncommon spreads of tuberculosis during pregnancy and (2) the quite frequent detection of active tuberculosis initially in women within a year of delivery. Twenty-one of 64 patients studied were found to have active tuberculosis within 12 months following delivery, while 19 were diagnosed during pregnancy by routine photofluorography, without which routine the diagnosis might not have been established until after delivery. In view of the relative frequency with which apical infiltrates are found in young women of child-bearing age, it is possible that the stability of these infiltrates may be affected by the strains of pregnancy. Perhaps it may be that the woman constitutionally fitted for motherhood and not harassed by social burdens may thrive on pregnancy even in the presence of tuberculosis; the woman not constitutionally fit may find tuberculosis too great a handicap to withstand during her pregnancy.

The physician would do well, then, to advise against pregnancy until the tuberculosis has become inactive. If pregnancy occurs, he should apply active therapy immediately, recognizing that the great majority of pregnancies can be conducted safely.

II. Delivery or Abortion

Hippocrates taught that phthsis is ameliorated by pregnancy; 19th and 20th century clinicians were impressed by the seeming worsening of the disease during and shortly after the delivery. Pulmonary function and endocrinological observations suggest certain mechanisms tending to cause progression of tuberculosis during pregnancy. A possible ameliorating influence is that the pregnant woman needs and gets more rest than before or after pregnancy.

It has been aptly said that the chief cause of disaster to the tuberculous woman is not the baby in the womb but the baby in the home. When the mother must care for the newborn child she has little time to care for herself. We learned in an earlier era that the woman who obtained a good pneumothorax for unilateral tuberculosis early in the course of her preg-

nancy seldom had difficulty and succeeded in inactivating her disease. Because of these conflicting considerations, the value of terminating the pregnancy of a tuberculous woman has always been uncertain. The most recent report of Schaefer et al sheds considerable light on this controversial section of the problem. Their observation that interruption of pregnancy does not favorably influence the course of tuberculosis is supported by their findings that three months after therapeutic abortion only 13 per cent of the aborted patients had improved as compared to 56 per cent of those who had spontaneous full term or premature deliveries. They suggest that possibly abdominal or vaginal hysterotomy fails to improve the end results of tuberculosis because the patients cannot be kept under surveillance after interruption of pregnancy and because estrogen may exert a favorable influence on the course of tuberculosis by retarding vascular permeability.

The patients studied in this series uniformly displayed amazing fortitude in the face of extremely adverse social and economic circumstances, seldom asking for interruption of pregnancy. So powerful was the effect of current therapy, that the great majority of the patients improved. A good example of the contrast is:

Case 7: L. S. S. Tuberculosis was diagnosed August 7, 1944 and she received only bed rest therapy. Her first child was born spontaneously in 1941. She left the institution April 22, 1946 apparently without active tuberculosis. She became pregnant and was delivered of her second child spontaneously in 1948 but her tuberculosis underwent reactivation in 1949. Drug treatment was started October 31, 1950 and continued through September 15, 1952. She was delivered of her third child June 8, 1952 using only local anesthetic. Follow-up examinations December 14, 1954 indicated that the tuberculosis was inactive.

As a routine procedure, therapeutic abortion cannot be recommended for the tuberculous woman. It will undoubtedly be true for a long time to come, that special indications will exist for terminating pregnancy. It is further true that as treatment for tuberculosis improves, and as the frequency of undetected tuberculosis diminishes, these indications will be progressively fewer. Therapeutic abortion is still indicated, but only in certain special cases wherein the life of the mother is jeopardized by the pregnancy. Failure of disease to respond adequately to therapy, severe drug reactions making chemotherapy impractical, excessive vomiting or other nutritional disturbances may at times warrant interruption of pregnancy. Such instances are few and should remind us that pregnancy is interrupted, not to improve tuberculosis *per se*, but only to remove what is now an unusual obstacle in the course of successful therapy.

III. Treatment of Tuberculosis during Pregnancy

In general the treatment for tuberculosis should proceed exactly as if the woman were not pregnant with few exceptions. Antibiotic therapy should be conducted as otherwise indicated; if the tuberculosis has been inactive at least two years, chemotherapy is unnecessary. If the disease has not been inactive that long, chemotherapy is needed. Apparently, the fetus is not adversely affected by antibiotics given to the mother. Bed rest should be used exactly as otherwise indicated. Excisional surgery is seldom performed during pregnancy, but has been done without causing spontaneous abortion, Artificial pneumothorax has been maintained without event throughout pregnancy, but pneumoperitoneum should be discontinued by the fourth month of pregnancy to avoid penetration of the uterus.

Case 8: E. W. was delivered of her first baby when 15 years old; January 12, 1949. When her baby was 26 months old, a routinely applied tuberculin patch test was positive; so the mother was examined and found to have an apical infiltrate March 1, 1951 by which time she was again six months pregnant. Immediately after delivery treat-

ment was started with antibiotics and pneumoperitoneum and was continued when she became an outpatient until May 16, 1952 at which time air embolism occurred; the patient (not known to be in her third pregnancy) aborted spontaneously May 27, 1952 a four and one-half month fetus. Chemotherapy was resumed, and at her most recent examination August 6, 1954 she was regarded as having inactive tuberculosis.

IV. Method of Delivery

1. *Duration of Labor.* Although it was previously taught that the second stage of labor should be rapidly shortened either by forceps or Caesarean section,[3] in this series of cases there was nothing to suggest that the duration of labor had any influence in the ultimate outcome of the disease.

2. *Type of Delivery.* While Caesarean section was used in a few patients because of obstetrical indications, they seemed to fare no differently than those delivered spontaneously. The means of delivery could not be shown to alter the course of tuberculosis in these 64 patients.

3. *Types of Anesthesia.* Various types of anesthesia were employed. On some occasions inhalational, on others, pudendal block was used while many were delivered without benefit of any anesthesia. Uniformly good postpartal results with only rare spreading of disease justify the attitude that type of anesthesia, mode of delivery and method of conducting delivery should be left to the obstetrician to handle exactly as he would do if the patient did not have tuberculosis.

V. Protecting the Baby

The best protection to the newborn baby is to prevent tubercle bacilli from reaching it. If the mother has been rendered sputum negative prior to delivery, protection is maximum. This can be accomplished either by closing cavities with some form of collapse therapy or by the use of antibiotics. Occasionally it is accomplished by excisional surgery although this is unusual. The mother should not nurse the baby for two reasons:

1. Contact between mother and baby should be broken until the mother has definitely reached the stage of inactive tuberculosis.

2. The mother should not have such responsibility until she is regarded as well enough to assume her domestic labors. The dangers of infection to the baby are well known and are real.

Repeatedly it has been demonstrated that the younger the child when a primary tuberculosis is established the graver the prognosis. Platou has shown that tuberculosis among infants and young children is a particular problem in this section of the country. The obvious method of prophylaxis is to insist that each pregnant woman have a chest x-ray film at the time of initial medical[4] examination. Preferably this should be repeated at the seventh month of the pregnancy although this of course is not always obtainable. Routine photofluorogram studies have shown that many young women have apical lesions. Only too often this form of examination is omitted and tuberculosis is not discovered until after the baby has been infected. The symptoms of early tuberculosis are notoriously few and misleading and, occurring in the post natal period, are all too apt to be ascribed to psychosomatic manifestations. The obstetrician has an excellent opportunity to apply the principles of preventive medicine here. Discovery of a lesion in the lung before it is big enough to produce symptoms can lead

to adequate study of the patient and the prevention of needless loss of health and life in mother and child.

SUMMARY AND CONCLUSIONS

Pregnancy does impose an additional stress for the tuberculous woman, a stress almost impossible to measure quantitatively or to evaluate statistically. Most women, particularly those anxious for children, can tolerate this stress today with the antibiotics currently available. To reduce this stress to the minimum, tuberculous women should be advised to defer pregnancy until the disease has been inactive at least two years if minimal, three years if moderately advanced, five years if far advanced. Experience with a relatively small group suggests that if this precaution is observed, even multiple pregnancies are tolerated without reactivation of the tuberculosis. To detect tuberculosis, each obstetrical patient should have a chest x-ray film examination as soon as pregnancy has been discovered. When tuberculosis is found in a pregnant woman, antibiotics and rest should be started at once precisely as during the nongravid state. Other methods of therapy should be added as needed. The patient may be truthfully reassured that with adequate therapy, she will continue to improve despite the pregnancy, may be delivered of a normal child by the same maneuvers that would be used if she did not have tuberculosis, and will be noninfectious by the time of confinement.

RESUMEN Y CONCLUSIONES

El embarazo impone a la mujer tuberculosa un desgaste adicional casi imposible de estimar cualitativamente o devaular estadísticamente. La mayoría de las mujeres, sobre todo las que ansían tener hijos, toleran este desgaste con los antibióticos hoy disponibles. Para reducir este desgaste al mínimo las tuberculosas deben ser acon sejadas para que difieran el embarazo hasta que la enfermedad sea inactivada por dos años en las formas mínimas, tres años en las moderadamente avanzadas y cinco años en las muy avanzadas. La experiencia con un grupo reducido sugiere que si estas precauciones se toman aún los embarazos múltiples son tolerados sin reactivación de la tuberculosis.

Para descubrir la tuberculosis cada embarazada debe tener una radiografía de tórax tan pronto como se conoce que hay embarazo. Cuando la tuberculosis se descubre en una embarazada, los antibióticos y el reposo deben empezarse inmediatamente como durante el estado ingrávido. Los otros métodos de tratamiento pueden usarse según se necesiten. Debe asegurarse a la enferma que con tratamiento adecuado continuará mejorando a pesar del embarazo, que dará a luz un producto sano y mediante las mismas maniobras que se usarán sin tener tuberculosis y que para la época del parto ella será ya no contagiosa.

RESUME

Le grossesse impose un choc supplémentaire pour la femme tuberculeuse, et un choc presque impossible à évaluer quantitavement ou statistiquement. La plupart des femmes, particulièrement celles qui tiennent à avoir un enfant, peuvent supporter aujourd'hui ce choc, grâce aux autibio-

tiques couramment utilisés. Pour réduire ce choc au minimum, les femmes tuberculeuses devraient être avisées d'éviter une grossesse jusqu'à ce que la maladie soit inactive au moins pendant deux ans, si les lésions étaient minimes, trois ans si elles étaient modérément avancées, cinq ans s'il s'agissait de lésions très avancées. L'expérience des auteurs portant sur un groupe relativement restreint de malades, les amène à penser que si cette précaution est observée, des grossesses même multiples peuvent être tolérées sans réactivation de la tuberculose. Pour dépister la tuberculose chaque femme devrait être soumise à une radiographie pulmonaire aussitôt que la grossesse a été découverte. Lorsqu'on découvre une tuberculose chez une femme enceinte, un traitement par les antibiotiques et le repos devraient être commencés immédiatement, exactement comme pour les autres malades. D'autres méthodes de traitement peuvent être adjointes, si nécessaire. La malade peut recevoir vraiment l'assurance qu'avec un traitement approprié, elle continuera à s'améliorer malgré la grossesse, qu'elle a la possibilité d'accoucher d'un enfant normal par les mêmes méthodes qu'on utiliserait si elle n'était pas tuberculeuse, et que cet enfant ne sera pas contaminé au cours de l'accouchement.

ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNGEN

Die Schwangerschaft stellt eine zusätzliche Belastung für die tuberkulöse Frau dar. Diese Belastung ist quantitativ oder statistisch nicht messbar. Die meisen Frauen, besonders solche, die Kinder wünschen, können diese Belastung mit Hilfe der heutzutage gebräuchlichen Antibiotika vertragen. Um diese Belastung auf ein Minimum zu reduzieren, sollte tuberkulösen Frauen geraten werden, die Schwangerschaft so lange aufzuschieben, bis die Krankheit bei geringfügigem Befund mindestens 2 Jahre, bei mässig fortgeschrittenem Befund 3 Jahre und bei weit fortgeschrittenem Befund 5 Jahre inaktiv geblieben ist. Die Erfahrung bei einer relativ kleinen Zahl von Patientinnen lehrt, dass under Berücksichtigung dieser Vorsichtsmassregeln sogar mehrfache Schwangerschaften ohne Reaktivierung des tuberkulösen Prozesses überstanden werden. Um die Tuberkulose aufzudecken, sollte jede gravide Frau, sobald ihre Schwangerschaft festgestellt worden ist, einer Röntgenuntersuchung unterzogen werden. Ist eine Tuberkulose bei einer Graviden festgestellt, sollte sofort eine tuberkulostatische und Ruhe-Behandlung begonnen werden in derselben Form wie sie üblicherweise durchgeführt wird. Soweit erforderlich, sollten andere Behandlungsmethoden hinzugezogen werden. Die Patientin kann darüber aufgeklärt werden, dass bei einer regelrechten Behandlung die Besserung trotz der Schwangerschaft eintreten wird, und dass sie in der gleichen Weise von einem gesunden Kind entbunden werden kann wie es der Fall wäre, wenn sie keine Tuberkulose hätte, und dass sei zur Zeit der Niederkunft nicht ansteckend sein werde.

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A Rational Approach to the Diagnosis and Treatment of Pulmonary Heart Disease*

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Health authorities have become increasingly aware of the role of smoking and air pollution in the production of chronic bronchitis and emphysema, precursors of cor pulmonale. This has led us to make a study of etiology, diagnosis and treatment of pulmonary heart disease.

Flint[1] found cor pulmonale to be the commonest single cause of congestive cardiac failure in patients admitted to a general hospital, the number of admissions in England markedly increasing from November to April, suggesting the prevalence of respiratory infections during winter as a possible cause.

Cor pulmonale can be acute, subacute or chronic. The acute form is right ventricular enlargement due to pulmonary embolism, infarction, and possibly pneumonia. Pulmonary metastases with consequent arteriolar blockage sometimes give rise to a form called subacute cor pulmonale. The chronic type is usually implied when the diagnosis of cor pulmonale is made. In this form long standing obstruction or hypertension in the pulmonary circuit (e.g. emphysema, pneumokoniosis) is the cause of right ventricular hypertrophy. A small group of pulmonary hypertension of unknown etiology has been described in which no sign of emphysema or other pulmonary disease is present. On examination pure right ventricular failure—increased jugular venous pressure, a tender enlarged liver and dependent oedema are found. No sign of pulmonary oedema is detectable. A loud high-pitched split second sound can be heard and P pulmonale is usually seen in the electrocardiogram. There is normal arterial oxygen saturation with a high arterio-venous oxygen difference.

Confusion has arisen with the clinical entity described by Ayerza in South America. In his original description a patient was so cyanosed as to be almost black. Brenner (1935), however, concluded that there was no good reason for retaining the term Ayerza's disease as the published cases described nothing but cor pulmonale.

We have limited ourselves to the chronic type arising secondary to respiratory disease and are excluding from this discussion mitral stenosis and certain congenital cardiac lesions which are often included as causes of cor pulmonale.

Diagnosis

The diagnosis of chronic cor pulmonale is based upon:

1) The recognition of the underlying pulmonary disease.

2) The detection of right ventricular enlargement with or without cardiac failure.

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*Awarded third prize (tie), 1955 Essay Contest, American College of Chest Physicians.

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3) The exclusion of pulmonary hypertension due to valvular disease and other cardiac abnormalities.

History of bronchial asthma or chronic bronchitis is frequently elicited. Pulmonary tuberculosis, pneumokonioses or bronchiectasis are found more rarely. Gradually increasing breathlessness over the last year or so and recent swelling of the ankles are usual complaints. The patient does not often object to lying flat, orthopnoea being rare. He is frequently cyanosed.

On physical examination signs of emphysema are usually present: barrel shaped chest with little movement on respiration; kyphotic spine; apex beat impalpable; hyper-resonance with diminished cardiac and liver dullness; breath and heart sounds are faint and expiratory sound prolonged.

Warm extremities, increased pulse pressure and tachycardia suggest the presence of raised cardiac output.

The signs of systemic venous congestion will appear if cardiac failure supervenes, such as increased jugular venous pressure, ankle oedema, oliguria, hepatomegaly and sometimes ascites.

Should vasomotor collapse occur the blood pressure drops, the pulse is small and thready, cardiac output is diminished, and the skin is cold and clammy.

On radiological examination the underlying respiratory disease can often be detected. There may be widening of rib spaces, depression of the diaphragm and increased translucency as seen in emphysema (Fig. 1). Signs of other disease causing pulmonary hypertension, such as increased pulmonary markings, cavitation and silicotic nodules may be present.

Exaggeration of the hilar shadows due to enlargement of the main pulmonary arteries and their branches is a common feature.

FIGURE 1

FIGURE 2

Figure 1: X-ray film showing advanced emphysema and prominence of the pulmonary artery.—*Figure 2:* X-ray film of Case 2 showing enlargement of the heart with increase in the pulmonary artery shadow. Congestive changes in the lung fields and a little fluid at the right base are also present.

The earliest sign of right ventricular hypertrophy is enlargement of the pulmonary conus, best seen in the right anterior oblique position. Further increase in the conus is associated with enlargement of the main stem of the pulmonary artery. This will reflect itself as a definite bulge on the left border of the heart in the postero-anterior view. (Figs. 1 and 2). In advanced cor pulmonale enlargement of the right side may be obvious radiologically.

The earliest signs of the disease can be detected by cardiac catheterization when an increased right ventricular systolic pressure is found. On angiocardiography Sussman, Steinberg and Grishman have found in 24 of 28 unselected cases of emphysema dilatation of the base of the pulmonary artery or enlargement of the right ventricle with the interventricular septum convex to the left.

Other special investigations such as electrocardiograms often do not show characteristic changes of cor pulmonale. If these, however, are present, they are diagnostic. These changes are: Prominent peaked P waves (P pulmonale) in leads II, III and aVF; negative P wave in aVL; right axis deviation; vertical heart; clockwise rotation; and T_3 is often inverted. (See illustrations).

All these changes are typically present in the advanced stages of the disease, P pulmonale being the earliest sign of pulmonary hypertension to make its appearance.

Should further special investigation be indicated, the measurement of vital capacity and arterial puncture for the detection of central cyanosis will give abnormal results.

The progress of the disease and the detection of right ventricular enlargement can be illustrated as follows:

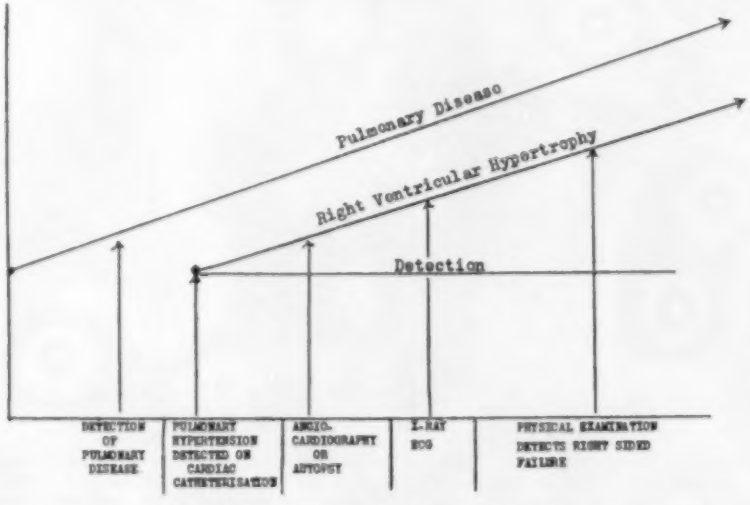

FIGURE 3: Diagnosis of Cor Pulmonale.

Differential Diagnosis:

Patients with emphysema who present themselves for treatment, pose the problem of determining the presence or absence of cardiac involvement. The exclusion of heart disease should only be made with confidence after special investigations, which should be repeated at frequent intervals, are negative.

It is sometimes difficult to distinguish pulmonary heart disease from other cardiac pathology of mixed etiology. Hyperkinetic circulatory states, particularly beri-beri in alcoholics, thyrotoxicosis and Paget's disease of bone in emphysematous subjects may have to be excluded.

Hypertension, being more common in emphysematous subjects than in the general population (Wood), poses the additional problem of differentiation between hypertensive and pulmonary heart failure and the possibility

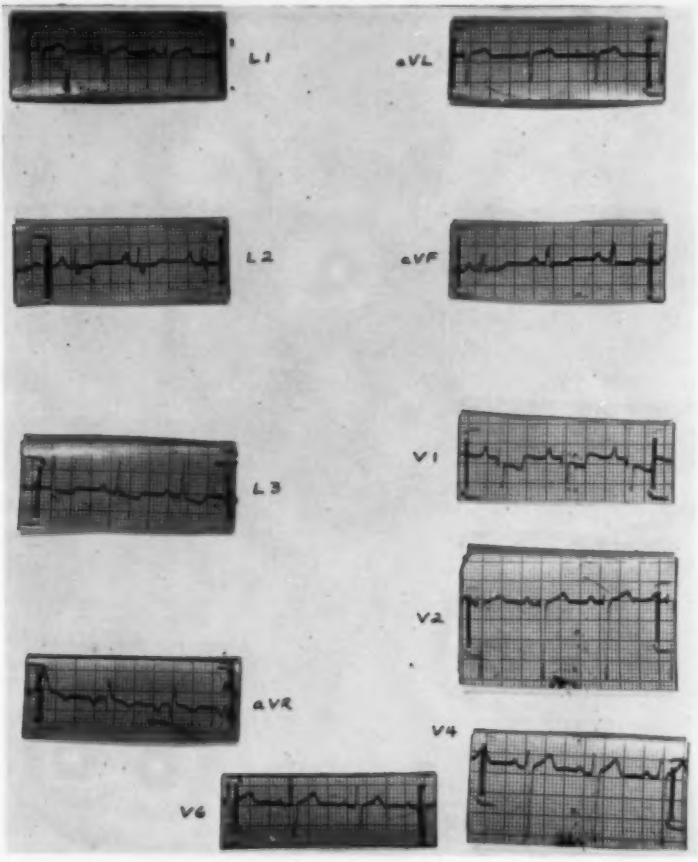

FIGURE 4: Electrocardiogram illustrating peaked P waves in L II, right axis deviation, vertical heart; clockwise rotation, and inversion of T_3. Further evidence of right ventricular hypertrophy is seen in V_1. From a case of cor pulmonale.

of both occurring together must be kept in mind.

Diseases such as mitral stenosis, atrial septal defect, mediastinal tumours and others to be differentiated. When a low blood pressure and reduced cardiac output—expressions of the last stages of cardiac failure or toxic vasomotor collapse from bronchopneumonia are present, it is difficult to make the correct diagnosis. Full investigation will usually make a distinction possible, but clinical impressions are often misleading.

Analysis of Hospital Records

Details of an analysis of the presenting clinical picture of patients admitted from July 1950 to June 1953 with the diagnosis of cor pulmonale and those in which characteristic post mortem changes of the disease were found are given in Table I.

TABLE I

	Emphysema	Pulmonary Tuberculosis	Bronchiectasis	Silicosis	Chronic Interstitial Pneumonia	Total	Per Cent
No. of cases	15	12	5	1	4	37	
Per cent	40	32	14	3	11		
Age							
0 - 20	0	0	0	0	0	0	....
21 - 40	0	3	3	0	0	6	17
41 - 60	6	7	1	0	2	16	43
61+	9	2	1	1	2	15	40
Sex							
Men	14	9	4	1	4	32	86
Women	1	3	1	0	0	5	14
Cough with sputum	15	12	5	1	4	37	100
Dyspnoea on admission	15	12	5	1	4	37	100
Swelling of legs							
Present	10	5	1	0	3	19	52
Absent	5	7	4	1	1	18	48
Raised JVP.							
Present	9	5	1	0	3	18	48
Absent	6	7	4	1	1	19	52
Cyanosis							
Present	9	0	4	0	4	17	46
Absent	6	12	1	1	0	20	54
Haemoglobin							
> 15	6	1	2	0	3	12	38
15 - 10	7	9	2	0	0	18	55
< 10	0	1	0	0	1	2	7
Not done	2	1	1	1	0	5	
ECG evidence of cor pulmonale							
Present	5	4	3	0	1	13	77
Absent	3	1	0	0	0	4	23
Not done	7	7	2	1	3	20	
X-ray evidence of cor pulmonale							
Present	9	1	1	0	4	15	60
Absent	6	3	1	0	0	10	40
Not done	0	8	3	1	0	12	

It will be seen that the commonest cause of cor pulmonale in this survey was emphysema. Figures closely corresponding with our own findings for age distribution and sex incidence were given by Wood—75 per cent were 50 and over, with a high preponderance among men.

Clinical symptoms such as cough, sputum and dyspnoea were generally complained of.

On special investigations such as electrocardiography and x-ray films, diagnostic changes of cor pulmonale were found in the majority of patients.

This series, being taken from hospital records, will not be indicative of signs and symptoms present in pulmonary hypertensive disease in the general community, since patients requiring hospitalization are usually in advanced stages of the disease.

Physiological Changes:

Diseases of the lung producing pulmonary arterial hypertension will give rise to cor pulmonale. The increase in pressure is brought about by

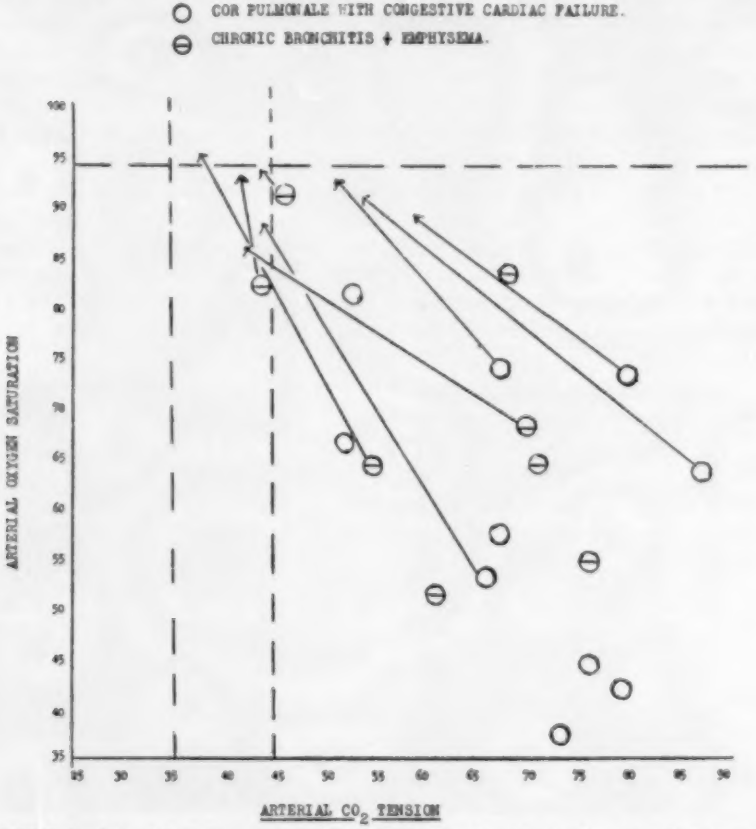
COR PULMONALE WITH CONGESTIVE CARDIAC FAILURE.
CHRONIC BRONCHITIS + EMPHYSEMA.
ARTERIAL OXYGEN SATURATION
ARTERIAL CO_2 TENSION

FIGURE 5: Arterial oxygen saturation and carbon dioxide tension on admission with and recovery from acute respiratory infection. Single points represent patients who died. (Redrawn from Westlake[3]).

a reduction in the capacity of the vascular bed due to fibrosis and destruction of lung substance, later being accentuated by structural changes in the pulmonary vessels such as atheroma and intimal thickening. The increase in the pulmonary arterial pressure is also influenced by the augmented cardiac output and the polycythaemia and hypervolaemia produced in response to the chronic anoxia.

Anoxaemia, hypercapnia and acidaemia present in cor pulmonale are due to reduced respiratory exchange and diminished maximum ventilatory capacity of the lungs. The decreased permeability and reduced area of the gaseous exchange surfaces and the shorter circulation time of the blood through the lungs are accentuating the anoxia and hypercapnia.

Westlake[2] defines chronic respiratory failure as the breakdown in the normal function of the respiratory centre to react to carbon dioxide retention and anoxia, which normally leads to hyperventilation and restoration of gaseous equilibrium. Accordingly, patients with cor pulmonale, with continuous anoxia and hypercapnia are in chronic respiratory failure.

This chronic failure, if interrupted by an episode of bronchopulmonary infection may change into acute respiratory failure. This is due to the inability of the respiratory mechanism to respond to the increased demands of pyrexia and anoxia caused by the infection.

The acute respiratory failure will accentuate anoxaemia, acidaemia and hypercapnia. The further course may be in either of two directions:

1) Commonly cardiac failure will supervene. In such cases it is due to the increased load on the heart produced by pulmonary arteriolar constriction caused by anoxia, and sodium and water retention. Also influencing the onset of failure is weakening of the heart due to myocarditis sometimes complicating the respiratory infection. The final stages in such patients are brought about by cardiovascular collapse with coma, falling

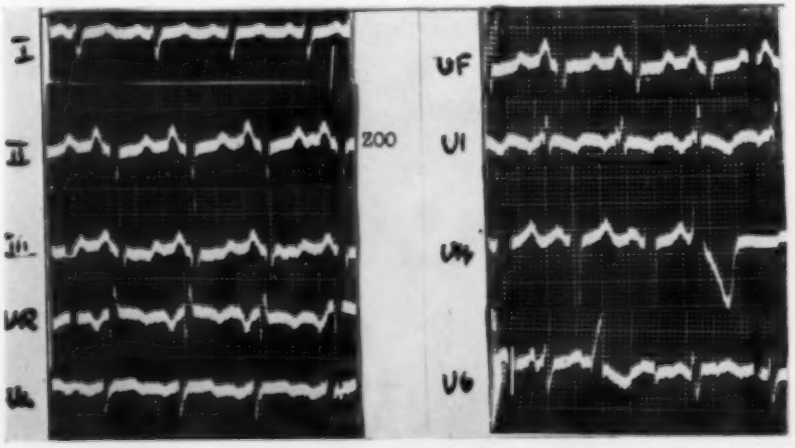

FIGURE 6: Typical changes due to cor pulmonale—P pulmonale, right axis deviation, vertical heart, evidence of right ventricular hypertrophy in precordial leads. There is sinus rhythm and occasional right ventricular extrasystoles.

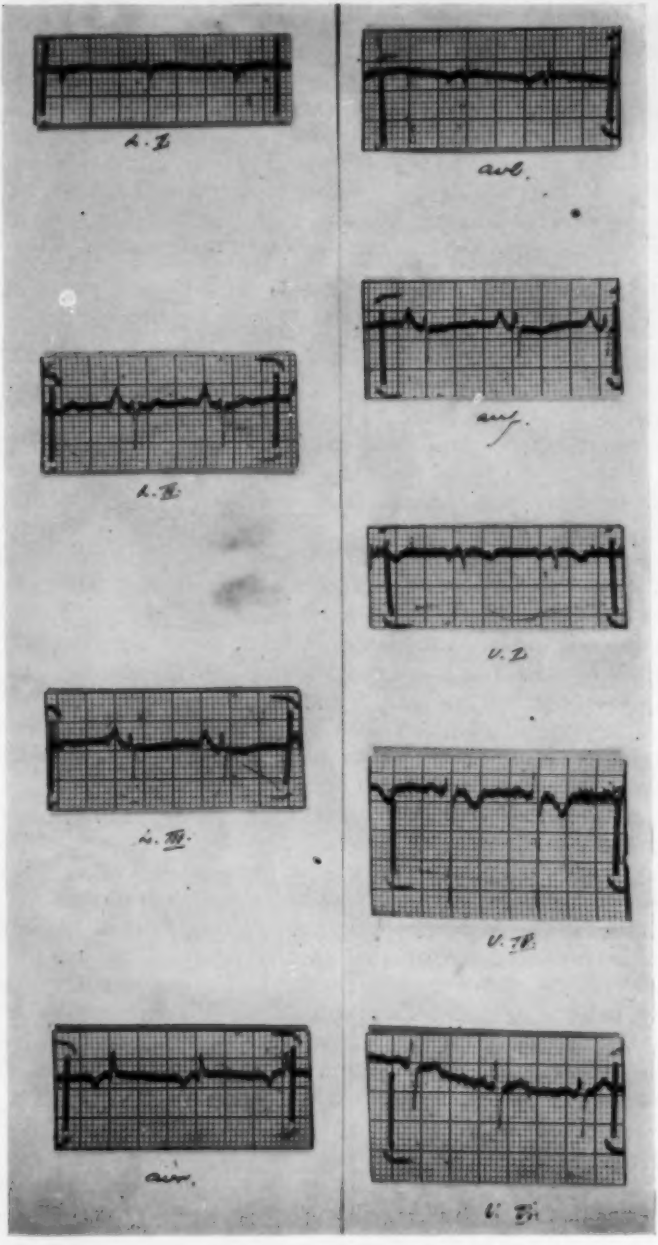

FIGURE 7: Electrocardiogram from a case of cor pulmonale, showing P pulmonale in L II, clockwise rotation, right ventricular pattern in all precordial leads. Inverted T wave in V, is suggestive of acute cor pulmonale.

cardiac output, peripheral vasconstriction, hypotension, diminished renal blood flow, uraemia and pulmonary oedema.

2) Some patients, constituting a minority, will present with warm extremities, increased cardiac output, and papilloedema and often complain of headache—the latter two being expressions of cerebral vasodilatation. Further increase of anoxia will produce disorientation, restlessness, delusions, hallucinations, myoclonic twitching and profuse sweating. The respiratory failure, if untreated, becomes rapidly progressive, low oxygen tension causing pulmonary oedema with further increase of anoxia (Drinker[3] 1945), this vicious cycle ending in asphyxiation.

Treatment

The foregoing physiological and biochemical considerations will point to a rational approach to the treatment of cor pulmonale.

In the compensated phase the treatment will be directed towards the maintenance of optimum gaseous exchange. This can be achieved by breathing exercises and postural drainage. The respiratory passages can be cleared of tenacious mucus by administration of aerosol mists of trypsin or synthetic detergents. Expectorants such as potassium iodide are also helpful. The usual bronchodilators are employed to relieve spasm. Of these, aminophylline is to be preferred because of its beneficial action on the coronary circulation. If these should fail in status asthmaticus, ACTH or cortisone can be employed.

In acute respiratory infections treatment must be directed towards the maintenance of the maximum oxygenation of the blood to prevent a rise in the pulmonary artery pressure. This is done by vigorous antibacterial treatment, administration of oxygen, bronchodilators and expectorants. Respiratory centre stimulants such as nikethamide may be used in the hope of maintaining adequate respiration.

Carbon dioxide narcosis can occur by suddenly relieving anoxaemia, the only remaining efficient stimulus to the respiratory centre. Therefore oxygen should be administered slowly at first, not exceeding 3 litres/min. Morphine, a respiratory centre depressant, is contra-indicated.

If cardiac failure arises as a complication, treatment of the respiratory infection is supplemented by that of the failure. The use of digitalis and other measures to lower venous pressure, has been seriously questioned by Howarth et al[4] (1947). They pointed out that the cardiac output is maintained at an optimum level under these circumstances. Any lowering in the venous pressure would cause a fall in the output of the heart and therefore interfere with oxygenation of the tissues. They further suggest that the use of diuretics, digitalis and low sodium diet may be of some use when oedema is extreme and a markedly raised jugular pressure is present, in the hope that the venous pressure may return to its optimal level. These investigators also condemn venesection as too drastic, which easily may have disastrous consequences.

Lately, however, the use of digitalis has been favoured again, its beneficial action on the heart itself outweighing any harmful effects which

might be caused by the lowered venous pressure.

Manifestations of respiratory infection can be masked by heart failure. Therefore, administration of antibiotics, usually penicillin, is of the utmost importance. Haemophilus influenzae, the common pathogen in bronchitis, is not affected by penicillin in the usual dosage; streptomycin or one of the tetracyclines are more effective.

Careful administration of oxygen is an essential part of the treatment, it having a beneficial effect upon the oxygenation of the blood and the pulmonary artery pressure.

Some observers advocate that if the arterial oxygen saturation remains below 80 per cent and the vital capacity continues to be critically low after removal from the oxygen tent, the administration of thiouracil may be considered as a means of reducing oxygen requirements.

Prognosis

The necessity of investigating presence or absence of cardiac involvement in emphysema and other diseases possibly leading to cor pulmonale, will result in the recognition of the condition many years before acute danger to life is present. With appropriate treatment the occurrence of congestive cardiac failure may possibly be delayed. Should, however, failure be manifest, the prognosis becomes poor, few patients surviving one year.

Prevention

The prevention of respiratory diseases causing emphysema will result in a diminished incidence of cor pulmonale in the community.

Consequently, measures directed towards decreasing the number of chronic bronchitics will have to be considered. Among those of preeminent importance is a reduction of air pollution. Although evidence that it produces chronic bronchitis is not conclusive, the occurrence of this disease in general practice is three to five times more common in polluted industrial towns than in other areas. Another etiological factor in the production of chronic bronchitis is smoking. So great are the difficulties in relinquishing this habit that no great fall in its incidence is to be expected. Other causes of bronchitis include diseased teeth and sinuses which should therefore immediately be attended to.

The prompt symptomatic treatment of asthma will delay the onset of cardiac involvement due to the production of widespread emphysema.

The prevention of other respiratory diseases such as bronchiectasis, pneumoconioses and tuberculosis should appreciably diminish the number of patients suffering from pulmonary heart disease.

Congestive cardiac failure in patients with cor pulmonale is usually caused by acute respiratory disease spread by droplet infection. This is markedly facilitated by overcrowded conditions existing in large cities. A beneficial effect might be expected with a reduction in the density of the population. The susceptibility of chronic bronchitics to acute bronchopulmonary infections is well known, and prolonged antibiotic treatment may prevent respiratory breakdown during winter months.

Illustrative Cases

Hospital admissions with cor pulmonale appear to us to fall into two broad groups, according to the predominating clinical features. Firstly, those admitted with acute bronchopulmonary infection, and secondly, those admitted in congestive cardiac failure.

An example of the first group is the following:

Case 1: Mr. C. B., aged 61, was admitted to hospital on August 5, 1950. He had been breathless on exertion for some months and developed bronchopneumonia a day before admission. On examination, he was dyspnoeic and cyanosed, had a markedly emphysematous chest, with a pulse rate of 84 and a blood pressure of 150/90. The apex beat was not palpable and the heart sounds were faint. Numerous râles and rhonchi were audible all over the chest. His temperature was 101° F.

On x-ray film one week previously, marked emphysema was found. A month before coming to hospital an electrocardiogram showed features of cor pulmonale.

He was treated with penicillin and digoxin. On August 7, 1950, his condition markedly deteriorated, cyanosis became worse, respiration rate increased further, and he died on August 8, 1950.

At autopsy, the lungs showed emphysema and bronchopneumonia. Marked hypertrophy of the right ventricle and dilatation of the right auricle were present. The tricuspid ring admitted four fingers and the left side of the heart was normal.

The following case is an example of the second group:

Case 2: Mr. J. G., aged 55, was admitted to hospital on March 10, 1951, complaining of shortness of breath for 12 months, cough and sputum for 40 years. He had several previous admissions to hospital in the past year. During the last 10 days he became dyspnoeic and his ankles swelled.

On examination, he was found to be cyanosed, becoming increasingly breathless while speaking. His venous pressure was raised. Heart sounds were faint, blood pressure 95/65. Pitting oedema of the ankles was present. There was an area of dullness to percussion over the right base posteriorly.

He was treated with mersalyl, digoxin, low salt diet, penicillin and oxygen. On March 12, 1951, his blood urea was 130 mgm. per cent, he was drowsy, had irritable cough with sputum, and the blood pressure was 125/80. On March 15, 1951, an x-ray film (fig. 2) showed the heart to be enlarged with prominence of the pulmonary artery, some congestive changes in the lung fields, and a little fluid at the right base was also present. On March 19, 1951, his haemoglobin was 17.1 gms. per cent, white cell count 6,900/c.mm. His jugular venous pressure was three and one-half inches above the clavicle. On March 20, 1951, he became very cyanosed, dyspnoeic, comatose, and died.

At autopsy, both lungs showed compensatory emphysema and marked congestion. The tricuspid ring admitted eight fingers and the right ventricle was hypertrophied and dilated. The right auricle was normal, the pulmonary artery was larger than the aorta. The left atrium was normal, the mitral ring admitted four fingers, and the left ventricle was slightly dilated. The liver showed chronic venous congestion and had a slight nodular appearance as of early cirrhotic changes. The spleen was also chronically congested.

CONCLUSION

It should be realised that the diagnosis of cor pulmonale on physical examination can be made only in advanced cases. Its presence should be suspected in any patient with chronic respiratory disease. Further investigations should be undertaken if clinical evidence is not yet at hand.

Prevention and prompt treatment of acute respiratory infection is the main aim in the management of patients with cor pulmonale. Should cardiac failure be present, administration of antibiotics is an essential

part of treatment. Oxygen therapy must be carried out with due regard to the possibility of carbon dioxide narcosis supervening.

Our thanks are due to the General Superintendent of our teaching hospital for permission to use records and to the physicians who allowed us to quote their cases.

RESUMEN

Debe tomarse en cuenta que el diagnóstico de cor pulmonale basado en examen físico sólo puede hacerse en casos avanzados. Su presencia debe sospecharse en todo paciente con enfermedad respiratoria crónica. Investigaciones posteriores deben llevarse a cabo si no se tiene todavía a mano evidencia clínica.

La prevención y el tratamiento rápido de la infección respiratoria aguda es el objetivo principal en el tratamiento de pacientes con cor pulmonale. Si se presentara insuficiencia cardiaca, la administración de antibióticos sería parte esencial del tratamiento. La oxígenoterapia se debe llevar a cabo teniendo en cuenta la posibilidad de que la narcosis con bióxico de carbono sobrevenga.

SCHLUSSFOLGERUNGEN

Es muss besonders betont werden, dass die klinische Diagnose des Cor pulmonale nur in fortgeschrittenen Fällen möglich ist. An das Vorliegen eines Cor pulmonale sollte man bei allen Patienten mit chronischen Atembeschwerden denken. Man muss auch dann weitere Untersuchungen durchführen, wenn die klinische Diagnose noch nicht sicher ist.

Die Verhinderung und schnelle Behandlung akuter Infektionen des Respirationstraktes ist das Hauptziel bei Patienten mit einem Cor pulmonale. Bei Vorliegen von Herzschäden ist die Anwendung von Antibiotika ein wesentlicher Teil der Behandlung. Die Sauerstofftherapie muss besonders im Hinblick auf die CO_2-Überladung durchgeführt werden.

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Three-Year Post-Discharge Status of Patients with Pulmonary Tuberculosis, Treated 1947 Through 1951

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The gratifying results obtained through the use of anti-bacterial agents in the treatment of pulmonary tuberculosis has stimulated many of us to forsake some of the older modalities of treatment. Thus the indications for pneumothorax and phrenemphraxis have become ever more restricted, and even pneumoperitoneum and thoracoplasty are employed less and less commonly. More recently, the need for bed rest has been questioned, and the use of hospitalization only for surgical operations has been discussed clandestinely by enthusiastic practitioners of phthisiology. Because this happy period has been of extremely rapid transition, with comparatively little published[1, 2, 3] concerning the longer term trends resulting from the ever increasing use of chemotherapy in pulmonary tuberculosis, this follow-up study is submitted.

From January 1, 1947, through December 31, 1951, 544 patients with pulmonary tuberculosis received their first discharge from the Pulmonary Disease Section of Veterans Administration Medical Teaching Group Hospital. The patients were war veterans, overwhelmingly male, approximately twice as many white as colored, and of ages consistent with participation in World Wars I and II. For the purposes of this study, only those with active tuberculous lesions of the lungs were included, and they were classified according to the year of their first discharge from our hospital. They consist of 220 who had reached maximum hospital benefit, 173 who left the hospital irregularly or for nonmedical reasons, 127 who were transferred to other institutions, and 24 who were discharged through death. A breakdown of these figures according to the year of discharge, is given in Table I. Of the 520 who left alive, it was possible for us to obtain follow-up information, three years after each patient's discharge, on 505 or approximately 97 per cent. This was accomplished by sending each patient, three years after the date of discharge, a simple form letter (Fig. 1) which inquired into the condition of health, ability to work, and medical adviser's name. If no answer was obtained, inquiries were made among the various Veterans Administration and local health agencies until the patient was traced and the desired information obtained. Answers were checked with their reported physicians, whenever possible.

It is probably desirable at this point to define the meanings of the terms used in our classification. Patients who were discharged as having reached maximum hospital benefit (MHB) had almost invariably reached these minimum standards, chest roentgenograms stable and without cavitation for six months, sputum smears consistently negative for six months, and

From the Pulmonary Disease Division, Medical Service, Veterans Administration Medical Teaching Group Hospital (Kennedy).

TABLE I
TYPES OF DISCHARGE, BY YEAR OF DISCHARGE

Year	1947	1948	1949	1950	1951
Total	81	79	143	112	129
MHB	17	23	61	49	70
Irregular	23	14	40	44	52
Transfer	35	40	34	13	5
Died	6	2	8	6	2

sputum or gastric cultures negative for three months. Irregularly discharged were those who left the hospital against medical advice, absconded, or were discharged for reasons of hospital discipline before they had reached the status required for an MHB discharge. This group therefore includes patients in all stages of activity and treatment. Those discharged by transfer fall largely into two groups. The great majority had concluded active therapy, had reached the stage of cavity closure and negative sputa, and thus were ready for convalesence. Because of our limited facilities for convalescent patients during 1947-48, many were transferred either to another Veterans Administration installation in Memphis, which had been especially designated for the treatment of tuberculosis, or to the rehabilitation center at Swannanoa, N. C. Another sizable group of patients were transferred to hospitals nearer their homes either because their disease appeared to be terminal, or personal problems or concomitant non-tuberculous disease seemed to make such transfer desirable. The deaths include all who had active pulmonary tuberculosis at the time of

VETERANS ADMINISTRATION
Medical Teaching Group
Kennedy Hospital
Memphis 15, Tennessee

Dear

We continue to be interested in you, and we would appreciate it if you would take the time to fill in the answers to the following questions and return to us:

1) Do you feel well?
   If not, what do you complain of?
2) Are you at home?
   If not, are you at a hospital or sanatorium? Which one?
3) Are you working? Since when? Doing what?
   Regularly? How many hours a day?
4) Are you being checked medically?
   How often? Where?
   What was the result of your last x-ray? When?
   What was the result of your last sputum exam? When?
5) Are you receiving any collapse treatment? Which?
6) Have you been ill since discharge from Kennedy? With what?
   When? Where were you treated?
7) Where could we obtain further medical information about you if we think it necessary?
8) Any further remarks you would like to make:

The enclosed envelope needs no postage. Trusting that you are well, and that you will let us hear from you soon.

Yours truly,
SAMUEL PHILLIPS, M.D.
Chief, Tuberculosis Section

FIGURE 1

TABLE II
FOLLOW-UP ALL PATIENTS, THREE YEAR POST-DISCHARGE

Year	No. Patients Followed	Well Per Cent	Sick Per Cent	Dead Per Cent
1947	74 (of possible 75)	58	19	23
1948	74 (of possible 77)	68	22	11
1949	134 (of possible 135)	52	34	13
1950	98 (of possible 106)	58	27	15
1951	125 (of possible 127)	67	20	13
Total	505 (of possible 520)	60	25	15

death, although other significant disease may have been present terminally. Thus the deaths include two who also had cancer of the larynx, and one who had polycystic disease of the kidneys.

Our follow-up study revealed that of the 505, out of the possible 520, who left our hospital alive and whom we were able to contact, 60 per cent were well (1950 N.T.A. classification "inactive"), 25 per cent were sick with active or recently active tuberculosis, and 15 per cent had died, (Table II). What seemed of most interest, however, at this time, was to learn whether those who had received chemotherapy had fared any better than those who had been treated with "merely" bed rest to which temporary or permanent collapse measures had been added as seemed indicated. At first glance, the results in 1951 when 71 per cent received chemotherapy were considerably better than in 1947 when only one in the entire group was so treated, (Table III). Such a comparison, however, is not valid as only 17 (21 per cent) received MHB discharges in 1947, whereas 70 (54 per cent) received MHB discharges in 1951. If there is any advantage in a patient remaining in hospital until he is ready medically for discharge, then the group which contains the greater proportion of MHB discharges should fare the better.

To obtain an answer of greater significance, therefore, we have compared all MHB discharges who received chemotherapy with all MHB discharges who did not (Table IV). Our MHB group consists of 217 patients, out of possible 220, making for a successful follow-up of 99 per cent. The figures indicate that those who received chemotherapy have indeed fared slightly

TABLE III
ALL DISCHARGES (1947-1951)
CHEMOTHERAPY EMPLOYED IN TREATMENT

Year	Per Cent Patients
1947	1
1948	18
1949	32
1950	38
1951	71

TABLE IV

MHB DISCHARGES (1947-1951)
PATIENT'S STATUS THREE YEARS POST-DISCHARGE

	Chemotherapy Used In Treatment	Chemotherapy Not Used
No. of Patients	73	144
	Per Cent	Per Cent
Well	92	79
Sick	4	16
Dead, All Causes	4	5
Relapsed	27	31
Working	60	53

better than those who did not. Greater proportions of such patients are well and working, and fewer are sick. Most significant, however, is the findings that the relapse rate in both groups is about the same, 27 per cent and 31 per cent.

If we examine our irregularly discharged patients in a similar manner (Table V), we find that apparently those who received chemotherapy fared slightly worse than those who did not. Whether the prompter relief of symptoms seen with streptomycin led those so inclined to leave the hospital earlier than similar patients who did not receive this drug, it is difficult to say. But in view of the large numbers of tuberculous patients who leave hospital for non-medical reasons, this observation may be of some significance.

Of interest also is a comparison between the status, three years after leaving hospital, of all patients who were discharged as having received maximum hospital benefit and all those who left irregularly. The differences are marked, 83 per cent MHB patients well as compared to 37 per cent, 12 per cent sick as compared to 42 per cent, and 5 per cent dead as compared to 21 per cent (Table VI). These differences are much greater and probably more significant than the slight differences we noted between patients who received chemotherapy as part of their treatment and those who did not.

Discussion

The above findings appear to indicate that the type of discharge a patient receives will determine to a great extent his physical condition

TABLE V

IRREGULAR DISCHARGES (1947-1951)
PATIENT'S STATUS THREE YEARS POST-DISCHARGE

	Chemotherapy Used In Treatment	Chemotherapy Not Used
No. of Patients	68	95
	Per Cent	Per Cent
Well	32	41
Sick	46	39
Dead	22	20
Relapsed	50	49
Working	16	21

TABLE VI
COMPARISON OF STATUS THREE YEARS POST-DISCHARGE

Type Discharge	MHB	Irregular
No. of Patients	217	163
	Per Cent	Per Cent
Well	83	37
Sick	12	42
Dead	5	21
Relapsed	29	50
Working	56	20

and the status of his pulmonary tuberculosis, three years later. They also suggest that the method of treatment used while the patient is hospitalized is not too important provided that it was effective. Those who did not receive chemotherapy and were able to achieve discharge with the more conservative methods of treatment got along almost as well as those who did. Of course, there are other factors to be considered. During the years under study, 1947-1951, patients who were found to respond satisfactorily to bed rest and to the various collapse measures were not usually given chemotherapy. In contrast, those who failed to respond and whose pulmonary tuberculosis continued to progress or at best remain stationary, were considered proper cases for streptomycin, etc. The drugs when used, usually were given singly and for comparatively short courses, 120 days or less. Perhaps, then, the fact that such patients treated in this fashion, could equal the results obtained with more favorable patients, is evidence of the superiority of the post-discharge results of chemotherapy. At any rate, it is probable that multiple drug therapy for prolonged courses may influence the post-hospital period of patients treated for pulmonary tuberculosis, even more obviously for the better. What attracts our attention, however, is that the patients treated with chemotherapy relapsed just about as frequently as those who had only bed rest and collapse measures. Thus our follow-up gives no indication that chemotherapy has succeeded as yet in changing the relapsing nature of pulmonary tuberculosis. It does suggest that enthusiasm aroused by early success in treatment must not beguile us to leap to the assumption of permanent control of the disease, and that tried and proved procedures should not be discarded lightly until the evidence is definite that they are no longer needed.

Appreciation is expressed to Mrs. Jane Gibson, whose untiring efforts were responsible for the high proportion of successful follow-ups attained.

SUMMARY

1. A follow-up of 505, of a possible 520, patients with pulmonary tuberculosis treated during the period between 1947-1951, and studied three years post-discharge is presented.

2. The type of discharge received was the most important factor in determining the patient's status three years post-discharge.

3. Whether the patient received chemotherapy or not prior to discharge,

seemed to be of minor importance to the post-hospital course.

4. The fact that patients who received chemotherapy were as a group less favorable cases than those who did not, may account for the lack of obviously superior post-discharge results. It is suggested that chemotherapy may have made it possible for the more gravely ill patients to achieve similar results as the more favorable patients.

5. It would appear, also, that chemotherapy as used in 1947-1951 did not significantly alter the tendency of tuberculosis to relapse.

6. Tried and proved methods of therapy should not be discarded until evidence accumulated over a sufficiently long period of time definitely indicates that they are no longer needed.

RESUMEN

1. De 520 enfermos posibles de seguirse, se presenta el estudio de 505, que sufrieron tuberculosis pulmonar, que se trataron entre 1947 y 1951 y se pudieron seguir por tres años después de susalida.

2. El tipo de alta fué el factor más importante para determinar la situación del enfermo tres años después.

3. Para la evolución fuera del hospital fué de importancia menor el que el enfermo se hubiese sujetado a quimioterapia o no antes de su salida del hospital.

4. El hecho de que los enfermos que recibieron quimioterapia hayan sido como grupo, menos favorables que aquéllos que no la recibieron, puede ser la causa de la falta de mejores resultados después de su salida. Se sugiere que la quimioterapia puede haber hecho posible para los casos más graves lograr resultados similares a los de los enfermos menos graves.

5. Parecería también que la quimioterapia como era usada de 1947 a 1951 no alteró de modo significante la tendencia de la tuberculosis a las recaídas.

6. Los métodos probados como eficaces no deben descartarse hasta que no reúna la evidencia por un tiempo suficientemente largo de que ya no se necesitan.

RESUME

1. L'auteur présente un contrôle portant sur 505 malades, peut-être même 520, atteints de tuberculose pulmonaire de 1947 à 1951 et suivis pendant trois années après leur sortie de l'Hôpital.

2. C'est sur le caractère du bulletin de sortie accordé au malade que l'on put déterminer de la façon la plus valable l'état du malade trois ans après la sortie.

3. Le fait que le malade ait reçu ou non de la chimiothérapie avant sa sortie semble être un facteur de moindre importance pour le contrôle après la sortie de l'Hôpital.

4. Les malades qui furent soumis à la chimiothérapie constituaient un groupe de cas moins favorables que ceux qui n'en reçurent pas. Ceci peut entrer en ligne de compte pour expliquer l'absence de résultats nettement

supérieurs lors de la sortie de l'Hôpital. L'auteur émet l'opinion que la chimiothérapie peut avoir aidé les malades plus gravement atteints à acquérir des résultats semblables à ceux obtenus chez les malades les moins atteints.

5. Il peut apparaitre également que la chimiothérapie telle qu'elle était utilisée en 1947-51, n'aidait pas énergiquement la tendance de la tuberculose à régresser.

6. Des méthodes éprouvées de traitement ne devraient pas être éliminées avant qu'une expérience portant sur une période de temps suffisamment longue n'ait définitivement indiqué qu'elles ne sont plus nécessaires.

ZUSAMMENFASSUNG

1. Von 520 Patienten, die in den Jahren 1947-1951 wegen Lungentuberkulose behandelt worden waren, konnten 505 3 Jahre nach der Entlassung nachuntersucht werden.

2. Die Art der Entlassung war von grösster Bedeutung für den Zustand des Kranken drei Jahre nachher.

3. Geringe Bedeutung für den Krankheitsverlauf nach der Entlassung aus dem Krankenhaus schien die Tatsache zu haben, ob der Patient vor der Entlassung Chemotherapie erhalten hatte oder nicht.

4. Dass die Patienten, die mit Chemotherapie behandelt wurden, keine besseren Ergebnisse aufwiesen, mag daran liegen, dass es sich hierbei um ungünstigere Fälle handelte. Es wird angenommen, dass die Chemotherapie bei schwerkranken Patienten ermöglichte, ähnliche Ergebnisse zu erzielen wie bei Patienten mit günstigeren Befunden.

5. Man hat ausserdem den Eindruck, dass die 1947-1951 verabreichte Chemotherapie nicht wesentlich die Neigung der Tuberkulose zu Rezidiven geändert hat.

6. Erprobte Behandlungsmethoden sollten nicht eher abgeschafft werden als über eine hinreichend lange Zeit der Beweis erbracht ist, dass sie wirklich nicht länger benötigt werden.

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Bacteriological Studies of Resected Pulmonary Tuberculosis Lesions

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Bacteriological studies were performed with materials obtained from excised solid cavitary tuberculous lesions, including bronchial and pneumonic secretions. Materials from these lesions were smeared and cultured by a standard and additional techniques for tubercle bacilli in order to determine whether they were viable following chemotherapeutic regimens.

Viable tubercle bacilli were obtained in over half of the total cases studied. Upon obtaining the positive cultures from the resected lesions, further susceptibility studies were performed and compared with the preoperative findings determined on the sputum and gastric cultures.

Laboratory Examinations

The solid lesions were enucleated and the cavities were sectioned for bacteriologic examinations. Materials obtained from small foci or clusters were handled separately. Fresh bronchial and pneumonic secretions were also examined.

Direct smears were made from all of the materials studied. The "cold" staining technique (modified), based on the original Kinyoun method, was used. The materials from solid lesions and cavity walls were then macerated. Dubos and TB broth base† media were used as a diluent during this procedure. This homogenized material was placed in approximately 30 cc. of Dubos and/or TB broth base containing 0.5 per cent albumin (bovine fraction) and 25 units of penicillin per milliliter. In a few days this was centrifuged and a portion of the sediment or apparent growth was subcultured onto Jensen-Lowenstein medium, with the remaining material in liquid medium being resuspended. These cultures were kept until positive, or for a period of at least three months. Positive cultures were used for the drug susceptibility determinations.

In addition to the above routine media used, additional variations in medium were incorporated from time to time, including blood agar-penicillin, A. T. S., Jensen-Lowenstein (containing neotetrazolium chloride), and charcoal agar, with no overall apparent advantage over the routine procedure used.

The addition of albumin wash to our routine and surgical studies has not increased our number of positive findings in over 6,000 cultures to date, so we see no particular advantage in its use.

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†TB broth base without polysorbate 80, as prepared by B. B. L., Baltimore, Md.

TABLE I
BACTERIOLOGICAL SUMMARY OF PULMONARY RESECTIONS FOR TUBERCULOSIS

	Number	Per Cent
CASES: (60)		
Cases with positive smears	48	(80)
Cases with positive cultures	37	(62)
Cases with cavities	26	(43)
(7 cases had 2 cavities each)		
(3 cases had 3 cavities each)		
LESIONS: (216 smears: 214 cultures)		
Lesions with positive smears	137	(63)
Lesions with positive cultures	75	(35)
Pos. smear and neg. culture	71	(33)
(65 solid and 6 cavities)		
With neg. smear and pos. culture	12	(6)
(10 solid and 2 cavities)		
SOLID LESIONS: (178)		
Positive smears	107	(60)
Positive cultures	50	(28)
CAVITIES: (38)		
Positive smears	30	(79)
Positive cultures	25	(66)

PRE-OP. CHEMOTHERAPY AND POST-OP. BACTERIOLOGY

Pre-Op. Chemotherapy	No. of Cases	Pre-Op. Pos. Sputum/Gastric No.	Per Cent	Cases with Cavities No.	Per Cent	Cases with Pos. Smears No.	Per Cent	Cases with Pos. Cultures No.	Per Cent
0 - 4 mos.	11	3	(27)	3	(27)	9	(82)	7	(64)
5 - 8 mos.	18	8	(44)	9	(50)	13	(72)	11	(61)
9 - 12 mos.	17	3	(18)	4	(23)	13	(76)	7	(41)
13 - 18 mos.	6	3	(50)	3	(50)	5	(83)	4	(67)
19 - 25 mos.	8	6	(75)	7	(87)	8	(100)	8	(100)
TOTAL	60	23	(38)	26	(43)	48	(80)	37	(62)

Discussion

Many opinions have been expressed as to the status of organisms isolated from resected lesions.[1-7] The answer is not yet available. D'Esopo and coworkers believe that these organisms are forever avirulent and nonviable.[1] Auerbach sees no reason why one should feel that the bacilli are not at least potentially virulent.[3] Bacteriology of tubercle bacilli is not well understood. It has many peculiarities. The purpose of this paper is an attempt to add personal opinion (theorized) and to discuss and submit our findings.

Table I shows a summary of the 60 cases studied. Positive smears were obtained in 80 per cent, and positive cultures in 62 per cent. Cavities were demonstrated in 43 per cent.

A breakdown as to all lesions studied showed a 63 per cent average with positive smears, and 35 per cent cultures. The number of positive smears with negative cultures was 33 per cent, which included 65 solid and six cavity cases.

The number with negative smears and positive cultures was six per cent, which included 10 solid lesions and two cavities.

The 178 samples taken from solid lesions showed 60 per cent with positive smears and 28 per cent with positive cultures. Cavities gave a higher percentage of both positive smears, 79 per cent, and positive cultures of 66 per cent.

It is felt that the tubercle bacillus has been altered in its biochemical mechanism and viability, depending on the type of lesion, natural defense, numbers, and its ability to adapt (mutation). The alteration may be in the death of the bacillus and all degrees from death to viability. This is thought to be a stepwise process, as reflected in the time of growth and in the sometimes disagreement of the pathological and bacteriological findings. Certainly the "kill phase" is not instantaneous, using antituberculous drugs, nor are the results. In fact, the action is primarily bacteriostatic. Various products of the tubercle bacillus have been shown to give histopathological changes with no viable organisms present.

The bacteriological media used are somewhat empirical except for the basic carbon, nitrogen, and protein sources needed for the growth of the tubercle bacillus.

In order to completely answer this phase of the problem, we need to know the exact biochemical pathways or changes as reflected in the mutations innate or induced during chemotherapy. The lack of positive findings during chemotherapy certainly could not be based entirely on the deficiency of media as prior to chemotherapy many more positive cultures were obtained on the patients who were active, or at least were discharging acid fast bacilli, as were detected in positive smears. It is felt that keeping a culture for months to obtain a rare positive with one or two colonies may also be misleading and not necessarily helpful to the clinician. The patient serves as a good "test tube" during this period, and any spectacular clinical changes would show up on the follow-up cultural studies if spread or reactivity did occur, especially if the flora became "nonsusceptible" to the chemotherapeutics being used. Negative cultures (as now) obtained in the bacteriological procedures for tuberculosis do mean something even though they may reflect the effect on tubercle bacilli rather than the end, which is fundamentally the picture of tuberculosis. This effect with bodily response is many times the clinical cure. Surgery does not remove every minute nodule in the tuberculous lung, yet it rids most patients of detectable bacilli through excision of the cavity and other lesions, thus the purpose being the eradication of the greatest portion of the foci. The ideal situation develops in that the patient becomes sputum or gastric negative on culture and is clinically able to handle minute residual disease. Therefore, there is a trend toward resectional surgery of pulmonary lesions, with the aid of chemotherapy, meeting the surgical criteria.

Table II shows a comparison of preoperative susceptibility findings with the surgical material. Resistant populations of tubercle bacilli obtained from resected lesions were isolated in the cases where complete resistance was previously reported on cultures from gastric or sputum

TABLE II
COMPARISON OF SUSCEPTIBILITY FINDINGS FROM RESECTED LESIONS AND SPUTUM SAMPLES OBTAINED PRIOR TO SURGERY

Case No.	Treatment	Duration	Susceptibility (Sputum)	Susceptibility (Resected Specimen)
1.	SM-PAS-INH	16 weeks	SM-INH-PAS: PS	SM-INH: S PAS: PS & S } 2 samples
2.	SM-PAS	10 weeks	SM-INH-PAS: S	SM-INH-PAS: S (swab)
3.	SM-PAS-INH	30 weeks	SM-INH-PAS: PS	SM-INH: PS PAS: S & PS } 2 samples
4.	SM-PAS	14 months	SM-PAS: S; INH: PS	SM-INH-PAS: S
5.	SM-PAS	16 months	SM-INH-PAS: PS	SM-INH-PAS: PS—2 samples
6.	SM-PAS	5 months	SM-INH-PAS: S	Negative cultures
9.	SM-PAS	15 months	SM-INH-PAS: S	SM-INH-PAS: S—2 samples
15.	SM-PAS-INH	12 months	SM-INH: PS; PAS: S	Negative cultures
17.	SM-PAS	5 months	SM: NS; INH: S; PAS: PS	SM: NS; INH: S; PAS: PS
19.	SM-PAS-INH	16 months	SM-PAS: S; INH: NS	Negative cultures
21.	SM-PAS-INH	9 months	SM-PAS: PS; INH: S	SM-PAS: PS; INH: S
22.	SM-PAS	8 months	SM-INH-PAS: S	SM-PAS: S; INH: PS
24.	INH-PAS	11 months	None	SM-INH-PAS: S—2 samples
25.	SM-PAS	9½ months	SM: S	SM-INH-PAS: S
26.	INH-PAS	2 months	None	SM-PAS: S; INH: PS
27.	INH-PAS	3½ months	SM-INH-PAS: S	SM-INH-PAS: S
29.	INH-SM	4 months	None	SM-INH-PAS: S—2 samples SM-INH-PAS: PS
30.	INH-PAS-SM	9 months	None	SM-INH-PAS: S—2 samples
32.	SM-PAS	7 months	SM-INH: PS; PAS: S	SM-INH: PS—4 samples S—1 sample PAS: PS—5 samples

33.	SM-PAS	1 year	SM: PS; INH-PAS: S	SM-PAS: PS—2 samples INH: PS & S
34.	SM-PAS-INH	13 months	SM-INH: PS; PAS: NS	SM-INH-PAS: PS
35.	SM-PAS-INH	16 months	SM-PAS: PS; INH: S	SM-INH-PAS: S
36.	SM-PAS-INH	17 months	SM: NS; INH-PAS: PS	SM: NS; INH-PAS: PS
37.	SM-PAS	8 months	SM: PS; INH-PAS: S	SM: PS; INH-PAS: S
38.	SM-INH	8 months	None positive	SM-INH-PAS: S—4 samples
40.	SM-PAS	4 months	SM-INH-PAS: S	SM-INH-PAS: S
41.	SM-PAS-INH	4 months	SM-INH: S; PAS: PS	SM-INH: S; PAS: PS
42.	SM-INH	8 months	SM-INH-PAS: S	SM-INH: S; PAS: PS
45.	SM-PAS	1 year (interrupted)	SM-INH-PAS: S	SM-INH-PAS: S—3 samples
46.	SM-PAS	9 months	None positive	SM-INH-PAS: S
47.	SM-INH-PAS	1 year (+)	SM: NS; INH-PAS: PS	SM: NS; INH-PAS: PS
48.	SM-PAS	22 months	SM-INH-PAS: PS	SM-INH-PAS: NS
49.	SM-INH-PAS	24 months (interrupted)	SM-INH: PS; PAS: S	SM-INH-PAS: PS—3 samples
50.	SM-INH	7 months	SM-INH: S; PAS: PS	Negative cultures
51.	SM-INH-PAS	12 months	SM: NS; INH: ; PAS: PS	SM: NS; INH: S; PAS: PS
52.	PAS-INH	1 month	SM-INH-PAS: S	SM-INH-PAS: PS
53.	SM-INH-PAS	8 months (+)	SM-PAS: PS; INH: S	SM-INH-PAS: PS
56.	SM-PAS-INH	19 months	SM-INH-PAS: PS	SM: PS; INH-PAS: S
57.	INH-SM	16 months (interrupted)	SM-INH-PAS: S	SM-INH-PAS: S
58.	SM-PAS	12 months	SM-INH-PAS: S	No growth
59.	PAS-SM-INH-Viomycin	16 months (interrupted)	SM: NS; INH-PAS: PS	SM-PAS: NS; INH: PS
60.	SM-PAS	4-4½ months	SM: NS; INH-PAS: PS	SM: NS; INH-PAS: PS

TABLE III

No. of Cases	Treatment	Duration	Susceptibility (Sputum)	Susceptibility (Resected Specimens)
3 (1 non-TB)	SM-PAS	8 - 13 months	Negative	Negative cultures
15	SM-PAS-INH	6 - 19 months	Negative	Negative cultures

Note: 4+: Surface of medium entirely covered; 3+: Growth not quite confluent; 2+: Innumerable colonies; 1+: 50 to 200 colonies. Medium for susceptibility tests. Jensen-Lowenstein's modified.

Key to Table II:

A. Concentrations: SM: streptomycin—0, 10, and 100 mcgm./ml.
PAS: para-aminosalicylic acid—0, 1, 10, and 100 mcgm./ml.
INH: Nydrazid—0, 0.1, 1, 5, 10 mcgm./ml. (Isoniazid)

B. Susceptibilities:
S—Susceptible; no growth at
PS—Partial susceptibility; partial growth at
NS—Nonsusceptibility; equal growth with the control at

SM—10 mcgm./ml.of medium
INH— 5 mcgm./ml. of medium
PAS—10 mcgm./ml. of medium

examinations. These findings were similar to the original, as to population, with slight variations occurring when partial nonsusceptible (intermediate) variants were isolated, the nonsusceptible strains being isolated in the majority from the retreated cavitary disease which was not responding to chemotherapy. The overall interpretation and clinical application of susceptibility findings would not be affected by these slight variations as they occurred among the intermediate (mixed) variant populations.

Patients on chemotherapy prior to surgery who have been negative and who have an occasional positive culture containing a nonsusceptible strain will later become regularly positive on their present medical regimens, except for surgical intervention and/or with proper "new drug" coverage. This also seems to occur where the smear remains occasionally positive, with negative cultures over long periods and then the cultures become consistently positive.

In a small series of undiagnosed cases meeting the surgical criteria in which tubercle bacilli were cultured and who had never had positive findings prior to surgery, resistant organisms were not isolated even though treatment may have been for a considerable period. These were from tuberculous lesions that had been unchanged by chemotherapy from the first observation and were of long standing.

From the 60 cases presented in this study, only two have been found to have positive cultures on sputa or gastrics following surgery.

SUMMARY

1. Sixty-two per cent of the cases included in this study had positive cultures for Mycobacterium tuberculosis. Solid lesions gave 28 per cent, while cavitary lesions gave 66 per cent of the total positives obtained. Length of treatment had little effect on the number of positive cultures obtained on resection, this being affected somewhat by the nonsusceptible and persistent cavitary cases which were resected.

2. Chemotherapeutic susceptibility results in tuberculosis may vary slightly in the same individual, depending upon the type of lesion and source from which the tubercle organisms are obtained, as shown by our data comparing sputa or gastrics (preoperative) and resected material studied. These were noted where nonsusceptible (intermediate) variants occurred and, therefore, should not deter clinical interpretations of susceptibility findings.

Acknowledgement is made to Josephine Van Fleet, M.D., Pathologist, who cooperated by submitting these cases for bacteriological study and compiling the pathological data for Table I, and to Frank L. Jennings, M.D., Chief, Professional Services, whose constructive suggestions were appreciated in the preparation of this article.

RESUMEN

1. Sesenta y dos por ciento de los casos que comprende este estudio, tenían cultivos positivos de micobacterium tuberculosis. Las lesiones sólidas dieron 28 por ciento en tanto que las cavitarias dieron 66 por ciento del total de positivos obtenidos.

La duración del tratamiento tuvo poco efecto sobre el número de cultivos positivos en la resección, siendo esto algo afectado por la falta de susceptibilidad y la persistencia de la cavidad en los casos resecados.

2. Los resultados de la susceptibilidad terapéutica en tuberculosis peuden variar ligeramente en el mismo individuo dependiendo del tipo de lesión y del foco de donde se obtuvieron los bacilos como se observa en nuestros datos comparativos de los esputos y lavados gástricos (preoperatorios) y el material resecado.

Esto fué observado cuando se vieron variantes no susceptibles (intermedias) y por tanto no deben desalentar la observación clínica ante los hallazgos de susceptibilidad.

RESUME

1. 62% des cas compris dans cette étude donnèrent des cultures positives pour le bacille tuberculeux. Des lésions denses représentèrent 28% du total des cas positifs obtenus, tandis que les lésions cavitaires en représentèrent 66%. La durée du traitement a peu d'effet sur le nombre des cultures positives, obtenues à partir des pièces de résection. Ceci est dû en partie aux cavités persistantes et rebelles au traitement qui ont dû être traitées par exérèse.

2. La sensibilité chimiothérapique en tuberculose peut varier légèrement pour le même individu. Elle dépend de la lésion, et de l'origine des microbes, comme le montrent les auteurs par leurs constatations après comparaison des crachats et des tubages gastriques (avant l'opération) et des pièces d'exérèse. Ces résultats peuvent altérer les interprétations cliniques de la sensibilité.

ZUSAMMENFASSUNG

1. Bei 62% der in dieser Untersuchung einbegriffenen Fälle waren die Kulturen auf Mycobakterium tuberkulosis positiv. Bei soliden Herden waren es 28%, während cavernöse Veränderungen 66% der insgesamt

erzielten positiven Kulturen ergaben. Lie Länge der Behandlung hatte wenig Einfluss auf die Zahl der bei der Resektion erzielten positiven Kulturen; diese Zahl wurde jedoch etwas beeinflusst durch die unempfindlichen und persistierenden cavernösen Fälle, die zur. Resektion kamen.

2. Chemotherapeutische Empfindlichkeitsergebnisse bei Tuberkulose können bei demselben Einzelfall etwas variieren und zwar in Abhängigkeit vom Typ der Laesion und der Quelle, aus der die tuberkulösen Organismen gewonnen wurden wie aus unseren Werten zu ersehen ist, die Sputen oder Magensäfte (präoperativ) und das untersuchte Resektionsmaterial vergleichen. Diese Abweichungen kamen zur Beobachtung, wenn unempfindliche (intermediäre) Varianten auftraten, und sie sollten daher klinische Auslegungen von Empfindlichkeitsbefunden nicht verhindern.

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A Mild Outbreak of Tuberculosis in a Large Ontario Office

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The purpose of this paper is to present a report of an outbreak of tuberculosis which occurred in a group of 1200 office employees. The first case was discovered at the end of 1952, and others continued to appear until the middle of 1954. In 1950 and in 1954, Smith et al reported an outbreak of 27 cases of tuberculosis in a Nova Scotia community, involving mainly school children. The present report deals with the findings in a group of adults, and the number involved has been considerably smaller.

Prior to this outbreak, the organization had a tuberculosis control programme in effect, consisting of mass surveys for employees approximately every two years since 1947, and a pre-employment chest x-ray film service operating over the same period. Participation in the surveys was voluntary, but pre-employment chest films were compulsory. Both services were provided by the Gage Institute Chest Clinic. The medical department for this group was under the supervision of a competent registered nurse, but there was no physician on the staff. During the years in which mass surveys had been done, no active case of tuberculosis had been discovered as a result, but one active case was discovered through pre-employment chest films in November 1952. Until December 1952, no real tuberculosis problem existed as far as was known.

In making this report it has seemed advisable to deal with events in a chronological order, tracing the development of cases together with the control measures instituted.

On December 23, 1952, a male employee, age 21 (Case 1) was examined at the Gage Institute because a miniature film made a few days before on the advice of the office nurse, had shown marked abnormality. Far-advanced active pulmonary tuberculosis was diagnosed, and the patient admitted to a sanatorium in January 1953. Cavitation was present and several days later the Provincial Laboratory reported the sputum showed acid-fast bacilli on microscopic examination.

The question presenting itself was, of course, how did this patient develop far-advanced disease after a mass survey had been done at this office in February 1952? Investigation revealed that this employee had been transferred from another branch of the same organization in February 1952, and when transferred, had not been referred for a pre-employment film since a mass survey film at his previous place of employment in November 1951, was believed to have been normal. A careful search of all x-ray identification cards from this survey was done, but no record

Gage Institute Chest Clinic.

of this patient's film could be found. He gave a history of contact with tuberculosis several years before when an aunt in a Western Province had been treated in a sanatorium. The aunt may or may not have been the source of the disease, but no other contact with a tuberculous patient could be established.

This patient (Case 1), worked at one of a group of four desks which were arranged in pairs, so that their occupants faced each other with no space between the desks and the pairs were adjoining. Although possibly somewhat crowded, the working conditions were probably better than in many office buildings. About 120 employees worked on this floor which measured approximately 160 by 60 feet.

It was evident that there were a number of fairly close contacts and these employees were referred at once for screening films. Among those referred immediately, was a 24 year old female (Case 2) whose miniature film showed abnormality. Further investigation led to a diagnosis of "suspected pulmonary tuberculosis" and a recommendation for re-examination at an early date, but five weeks later, sputum which had been negative on smear, was reported positive on culture, and admission to a sanatorium was advised. She worked facing Case 1, separated by the width of the two desks.

Seated beside Case 1, was another young male Case 3, who also had a screening film early in January 1953, which was normal. On March 31, 1953, because he was not feeling well, he was again referred for a miniature film and this time an abnormal opacity was present. Immediately following this and before he could return for examination, he was transferred to a branch in another city where moderately advanced tuberculosis was soon diagnosed, but not before he had become a contact of a new circle of employees.

It is interesting to note that the fourth member of this group had changed on several occasions before these cases were discovered, and as far as can be determined, no one who worked in that position developed a lesion. Apparently these individuals received some protection through shorter periods of exposure and possibly through the slightly greater distance from the grossly infectious first case.

Perhaps the next (Case 4) should not come within the scope of this paper since contact did not occur at work, nor was the individual employed in the same office group, but the report would seem to be incomplete without reference to it. He was however, an employee at another branch of the same parent organization and had lived some time previously in the same rooming house with Case 1, where for a time they had been roommates. Considerable contact had occurred socially up to the time the first case was discovered. This 22 year old male had a normal x-ray film January 5, 1953. About April 5, 1953 after being transferred to a branch in another city, and thus starting another group of contacts, he was found to have active minimal tuberculosis, and was admitted to a sanatorium.

Case 5, was a 28 year old male who was employed in the same building, but on a different floor. He had, however lived with Case 1 some time previously and like the previous patient had continued to have considerable contact outside the office. On January 7, 1953, on another miniature chest film made for the same reason, abnormality was noted which led to a diagnosis of minimal active pulmonary tuberculosis. Later one specimen of sputum was reported positive on culture.

During this period, advice was sought and discussions were held with the Provincial and Municipal Departments concerned with tuberculosis control and the Division of Industrial Hygiene. These officials were keenly interested in the problem and gave valuable assistance. It was decided that the following steps were to be taken.

(1) A mass survey was to be done at once at which attendance should be compulsory. This was to be repeated in four months and again six months later, followed by further surveys as might seem indicated.
(2) The company was advised to obtain the services of a chest consultant to supervise the control programme.
(3) Tuberculin testing, to be done on a voluntary basis concurrently with a mass survey, was recommended.
(4) Employees were to be referred freely for chest films. This was to include not only the known relatively close contacts who were to be referred on a regular basis, but also employees desiring to have chest films at any time and employees presenting themselves at the medical department with complaints which might be due to tuberculosis.

During this period increasing tension was evident among the employees although efforts were made to allay fears as much as reasonably possible. A survey for all employees was done during the end of April and early in May 1953, and 974 of a total of approximately 1200 employees received chest films. Management made every effort to see that those who missed the survey were referred for films as soon as possible.

Among those who missed the survey because of absence through illness were two who proved to have significant findings.

One—Case 6, a 21 year old female was absent, under treatment at home for what was thought at first to be pneumonia. On May 6, 1953, she was able to attend the clinic and examination revealed moderately large pleural effusion presumed to be tuberculous. She worked about 60 feet from the original three cases until the end of 1952.

The other—Case 7, a 30 year old male had had a chest x-ray film as a contact April 15, 1953, which was normal. By May 8, 1953, he was a patient in a general hospital with massive pleural effusion considered to be tuberculous. He worked about 30 feet from the first three patients.

From the survey of April—May 1953, a 21 year old female (Case 8) was found on May 18, 1953 to have a minimal lesion considered probably active by the clinic and a private chest consultant. No contact could be

demonstrated with any of the other cases in the office, but there was a history of contact with an aunt who had been treated for pulmonary tuberculosis. The chest film of this patient had been normal in the February 1952 survey.

Case 9 was a 25 year old male who had lived with Case 1 for one month in 1951 and had continued to have frequent social contact with Case 2 and also Case 5. Films made as a contact in January 1953 and April 14, 1953, were negative, but while travelling in Europe in May 1953, he developed chest pain and fever, which soon subsided, and he did not have a chest x-ray film following this until the next mass survey, which was done in the latter part of August. This led to a diagnosis of pleurisy with effusion and admission to a sanatorium.

At the time this survey was done in August 1953, tuberculin testing was offered to all employees on a voluntary basis. In the survey 839 individuals received chest x-ray films, and an unrecorded number who missed the survey were referred for films afterward. Mantoux tuberculin tests using 1/20 mgm. of old tuberculin, were given to 850 persons. The numbers done in the various age groups together with the proportion of positive reactors are shown in Table I.

TABLE I

RESULTS OF TUBERCULIN TESTING OF EMPLOYEES

1. AUGUST 1953

Age Group	Number Done	Per Cent Reactors
Under 20	91	17.6
20 - 29	344	31.7
30 - 39	223	53.8
40 - 49	138	62.3
50 - 59	63	77.8
60 - 69	21	76.2
TOTAL	880	45

2. FEBRUARY 1954

Of 474 negative in August 1953, 400 received repeat tuberculin tests in February 1954. Four had converted and a fifth had a doubtful reaction.

Case 10 was a 27 year old male who had no known contact with any of the other cases. His miniature film in the April 1953 survey was normal on review. He was referred on October 20, 1953 for a chest film because he missed the survey in August. He had come from British Guiana in June 1951. His immigration film and pre-employment film were both normal, but in October 1953, he was found to have minimal, active pulmonary tuberculosis and sputum was positive on smear. He lived in a rooming house with several others from the same country, but investigation failed to reveal a source there.

Case 11 was a 23 year old female found to have slight abnormality in a film of November 30, 1953 after previous survey films had been negative. Periodic re-examinations were done and in July 1954, there were sufficient grounds for reaching a diagnosis of pulmonary tuberculosis, minimal, active, and admission to a sanatorium was advised.

A mass survey was done early in February 1954, when 909 received chest films, but there was no significant finding. At the same time, tuberculin testing was again offered to those previously negative and to new employees hired in the interval. Of the 474 negative to tuberculin at the first testing 400 were re-tested and four had converted. A fifth person showed a doubtful reaction. The number of converters is not greater than one might expect in the ordinary population.

Case 12 was a 26 year old female who was found to have minimal, active tuberculosis April 20, 1954. There was no demonstrable contact with any other of the cases, but it seems highly likely that she had received the infection from her mother, who died of a vascular accident while undergoing treatment in a tuberculosis hospital in another Province two years earlier.

Case 13 was a 36 year old female who had had exposure to Case 2 and several other cases and whose x-ray films made as a contact and routinely in the surveys, had shown no significant findings although she had been recalled for clinical examination after a film of November 1953. She changed places of employment, and on a pre-employment film of August 18, 1954, abnormality was noted which led to a diagnosis of tuberculous pleurisy with effusion and admission to a sanatorium.

During 1954, many contacts and many employees received chest films for various reasons, but no active disease has been discovered since August 1954. A survey in February 1955, failed to reveal any significant findings.

One other case deserves mention as it illustrates what might be termed a side product of the search for tuberculosis. A male, aged 62, was recalled for examination following a survey of this group in 1950. His film showed an abnormality which at the time was thought to represent an inactive tuberculous lesion of limited extent. He refused to return for further examination in spite of being advised it was desirable. He also missed the mass surveys of February 1952 and April 1953, but by then management was insisting that everyone receive a chest x-ray film, and he reported for a miniature film May 29, 1953. He was recalled for further examination, and it was obvious that there had been considerable increase in involvement since 1950. Further investigation revealed bronchogenic carcinoma. Pneumonectomy was done and the patient was able to return to work for a short period before retiring on pension.

Although no active case has been discovered since August 1954, miniature chest films are still being used freely in screening contacts and all employees presenting with symptoms which conceivably might be related to tuberculosis. The final outcome will not be known until considerable further time has elapsed. Of the four patients with positive sputum find-

ings the last exposure to other employees occurred in November 1953. With regard to Cases 8, 10, 11 and 12, no relationship could be established with the other cases discovered in the office. The possibility of contact having occurred at work has not been excluded since a number of the employees were not acquainted and contact could have occurred without their knowledge.

Management did a great deal to assist the employees involved by continuing salaries while they were off work, at full rates in the case of married and at half rates in the case of single employees. Alterations were made in the building to provide less close contact between employees at their desks, and an improvement was made in ventilation. The company played an important part in persuading employees to undergo tuberculin testing, and there was practically no objection to this procedure. Management also co-operated in a commendable manner in the distribution of information regarding the necessity of surveys.

SUMMARY

This report contains the findings to date in a group of approximately 1200 office employees where a case of far-advanced tuberculosis was discovered at the end of December 1952.

Definite contact was established for 11 months, and during the following 18 months, 12 additional cases of tuberculosis emerged. In four no relationship with the earlier cases could be established. In two of these four cases, it seemed likely that exposure had occurred from known outside sources while in two it was impossible to determine any likely source of infection.

The patients ranged in age from 21 to 36 years. Seven including the original occurred in males and six in females.

The first patient to be discovered had far-advanced disease. The subsequent cases consisted of one moderately advanced, seven minimal, and four of pleurisy with effusion. Pleurisy with effusion occurred in two males and two females.

With no further cases emerging, it is felt that adequate control will now be provided by making chest films of all new employees promptly, regular chest films of known contacts, and a continuation of the original programme of mass surveys at two-year intervals.

RESUMEN

Esta comunicación contiene los hallazgos hasta ahora en un grupo de 1200 empleados de oficina donde un caso de tuberculosis muy avanzada se descubrió al final de diciembre de 1952.

Se estableció claramente que había habido contacto por 11 meses y durante los siguientes 18 meses se descubrieron otros 12 casos de tuberculosis. En cuatro no se pudo establecer relación con el anterior. En dos de estos cuatro casos, parecía posible que la exposición haya tenido lugar con otras fuentes conocidas de afuera mientras que en dos fué imposible descubrir causa alguna como fuente de infección.

Los enfermos tenían de 21 a 36 años. Siete incluyendo el original eran hombres y seis mujeres.

El primer enfermo descubierto tenía tuberculosis muy avanzada. Los casos siguientes consistieron de: uno moderadamente avanzado, siete mínimos, y cuatro de pleuresía con derrame.

La pleuresía con derrame ocurrió en dos hombres y dos mujeres.

Ya que no han aparecido nuevos casos se cree que se provee ahora de un control adecuado mediante inmediatas radiografías de todo nuevo empleado, películas de tamaño normal en todos los contactos grupos cada dos años.

RESUME

Cette communication a pour but de présenter les constatations faites actuellement dans un groupe d'environ 1.200 employés chez lesquels un cas de tuberculose avancée fut découvert à la fin du mois de décembre 1952.

Des contacts certains avaient eu lieu pendant onze mois. Pendant les dix-huit mois suivants, douze cas nouveaux de tuberculose apparurent. Dans quatre d'entre eux, on ne put établir aucune liaison avec les cas antérieurs de tuberculose. Dans deux de ces quatre cas, il sembla que la contamination était survenue à partir d'origines extérieures connues, tandis que pour les deux autres malades, il fut impossible de déterminer l'origine de l'infection.

Les malades étaient âgés de 21 à 36 ans. Sept cas, y compris le cas initial, atteignirent des hommes et six cas des femmes.

Le premier malade découvert était porteur d'affection très avancée. Les cas suivants comprenaient une atteinte modérée, sept atteintes minimes et quatre cas de pleurésie avec épanchement. L'épanchement pleural atteignit deux hommes et deux femmes.

Aucune autre atteinte n'étant apparue, l'auteur estime que pour obtenir maintenant un contrôle efficace, il faut pratiquer dès son admission des radiographies pulmonaires à tout nouvel employé, exercer une surveillance radiographique pour tous les porteurs de lésions connus, et continuer le programme initial de contrôle systématique tous les deux ans.

ZUSAMMENFASSUNG

1200 Büroangestellte aus einem Betrieb, in dem 1 Fall von weit fortgeschhrittener Tuberkulose Ende Dezember 1952 aufgedeckt worden war, werden in diesem Bericht erfasst.

11 Monate lang bestand ein direkter Kontakt mit dem Kranken; 12 weitere Fälle von Tuberkulose wurden während dieser Zeit und während der folgenden 18 Monate herausgefunden. Bei vieren konnte keine sichere Beziehung zu der genannten Infektionsquelle gefunden werden. Bei zweien dieser Vier war es wahrscheinlich, dass die Infektion durch bekannte Bazillenträger ausserhalb des Betriebes erfolgte, während bei zweien ein sicherer Anhalt für eine Infektionsquelle nicht gefunden werden konnte.

Die Patienten waren 21-36 Jahre alt; 7 davon waren männlich (einschliesslich des Ersterkrankten) und 6 waren weiblich.

Bei dem zuerst entdeckten Kranken bestand eine weit fortgeschrittene Lungentuberkulose; bei den Infizierten war die Tuberkulose in einem Fall

mässig fortgeschritten, bei 7 Kranken geringfügig und bei 4 bestand sie in einer exsudativen Pleuritis. Die Pleuritis exsudativa trat bei 2 Männern und 2 Frauen auf.

Es wird für notwendig gehalten, sofort bei Eintritt neuer Angestellter in die Firma Röntgenaufnahmen anzufertigen, Leute mit bekannten Befunden regelmässig röntgenologisch zu kontrollieren und eine allgemeine Reihenuntersuchung in zweijährigen Abständen durchzuführen.

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Pulmonary Metastases*

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The development of pulmonary metastases is one of the gravest signs of the course of malignant disease. With their appearance, little can be done to halt the course of disease in the majority of cases, and the prognosis can usually be measured as a matter of months. Since they may be associated with but few symptoms and physical signs, chest radiography affords the most satisfactory method for their detection. Knowledge of their presence is as important to the physician in the management of the case, as it is to the surgeon, who can be saved unnecessary and even unwarranted operative measures.

It is therefore pertinent to assess the value of chest radiography as a means of diagnosing the presence of pulmonary metastases from all primary sources of carcinoma and sarcoma. This has been undertaken by correlating the chest x-ray film with the pathological material, in cases which were proved at autopsy to have pulmonary metastases.

Material

In the years 1944-1951 in this hospital autopsies were performed upon 465 bodies dead from cancer, and secondary lung deposits were demonstrated in 100 of them. These cases were found by search through post mortem records, and the patients' files were then consulted. The radiological and pathalogical correlation is based upon these 100 unselected cases of known lung metastases. As far as possible the chest x-ray chosen was the one taken just before death. In the great majority this was taken within a few days of the patient's death, and at longest it was three weeks previously (in one case).

Frequency of Pulmonary Metastases

Secondary deposits were found in nearly 22 per cent of all cancer post mortems. Table I indicates the range of primary sites of the carcinomata and sarcomata, together with the frequency of lung deposits from such sites.

Metastases may reach the lungs from the abdominal viscera via the portal vein and liver, or alternatively by the systemic circulation. Analysis of various malignant neoplasms indicates that metastases occur more frequently from sites whose dissemination would be expected to take place via the systemic circulation. Thus metastases occurred in over 30 per cent of cases in carcinomata of the larynx, thymus, breast, testis, kidney, thyroid, suprarenal, bone and fibrosarcomata. Conversely metastases were comparatively uncommon from sites which would be expected to disseminate along the portal vein and through the liver to the lungs. Thus carcinomata of the stomach, colon, rectum, pancreas and liver reached the lungs in less than a frequency of 30 per cent.

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*Awarded second prize, 1954 Essay Contest, American College of Chest Physicians.
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In making this broad and rough differentiation, the lymphatic route of dissemination of tumour cells has not been taken into account. Although this does, of course, play an important part in tumour dissemination, it is less so when considering pulmonary metastases. In some cases tumour cells probably reach the blood stream via the thoracic duct. Also involvement of the lung from bronchial, stomach and breast cancer is well recognized by this route in a direct manner. Lymphangitis carcinomatosa of the lung will be discussed later when considering the types pulmonary metastases.

TABLE I

Primary Organ	Number of Cancer Autopsies '44-'51	Number of Cases with Metastases	Percentage (Approx.)
Mouth and Tongue	18	3	17
Pharynx	9	2	22
Esophagus	20	2	10
Larynx	10	4	40
Bronchus	80	12	15
Thymus	5	2	40
Breast	29	14	50
Uterus and Cervix	38	5	13
Ovary	14	4	29
Prostate	5	1	20
Testis	6	5	87
Kidney	10	7	70
Bladder	25	3	12
Skin	9	1	11
Thyroid	8	3	38
Suprarenal	6	3	50
Bone	7	6	86
Fibrosarcoma	4	2	50
Other Systemic	9	2	—
Stomach	39	1	2
Colon	24	6	25
Rectum	18	3	17
Liver and Bile Channel	16	3	20
Pancreas	23	1	4
Lymph and Reticulum	31	5	15
TOTAL	465	100	22

Radiological "Visibility" of Metastases.

Chest radiographs demonstrated opacities, consistent with metastases, in 61 cases, and were apparently normal in the other 39 cases (Table II). In the accompanying table, the primary sites have been arranged to emphasize the predominantly negative radiological findings in tumours from certain sites. In examining such a series it would be unwise to make dogmatic deductions from this observation, since, as will be seen later, radiological visibility depends largely upon the size of the metastases. These were mostly small in the radiologically negative group.

TABLE II—Sites in Order of Decreasing "Visibility"

Primary Site	Number of X-Ray Positive Cases	Number of X-Ray Negative Cases	Total
Bladder	3	0	3
Pharynx	2	0	2
Synovioma	2	0	2
Skin	1	0	1
Prostate	1	0	1
Kidney	6	1	7
Testis	4	1	5
Bronchus	9	3	12
Ovary	3	1	4
Breast	10	4	14
Uterus and Cervix	3	2	5
Bone	4	2	6
Thyroid	2	1	3
Suprarenal	2	1	3
Mouth and Tongue	2	1	3
Larynx	2	2	4
Thymus	1	1	2
Colon	2	4	6
Liver	1	2	3
Lymph and Reticulum	1	4	5
Pancreas	0	1	1
Stomach	0	1	1
Esophagus	0	2	2
Fibrosarcoma	0	2	2
Rectum	0	3	3
TOTALS	61	39	100

Classification of Pulmonary Metastases

On the basis of autopsy findings, metastases were classified according to their size and number into five types:

Type A.: Miliary nodules up to 3 mm. in diameter.
Type B.: Scanty (up to 5) nodules less than 3 cm. in diameter.
Type C.: Numerous nodules present less than 3 cm. in diameter.
Type D.: Isolated large metastases over 3 cm. in diameter.
Type E.: Metastases replacing one lobe or more of a lung.

The number of cases belonging to each of these types, and whether they were radiologically visible, is analyzed in Tables III and IV.

Typical chest radiographs from each category are shown in Figs. 1-5.

TABLE III

Post Mortem Type of Metastases	Number of Cases
A	8
B	35
C	30
D	14
E	13
TOTAL	100

TABLE IV

Type of Metastases	Radiologically Positive Cases	Radiologically Negative Cases
A	4	4
B	7	28
C	23	7
D	14	0
E	13	0
TOTAL	61	39

Type A Metastases

In this series there were eight cases in which there was diffuse pulmonary involvement with small carcinoma seedlings. Chest radiographs showed diffuse miliary mottling in one half of the cases. The primary sites in the radiologically positive cases were: Bronchus (2), Breast (1), Colon (1), and of the radiologically negative cases were: Bronchus (1), Colon (1), Kidney (1), and Stomach (1).

Miliary carcinomatosis of the lungs may be by lymphatic or blood borne spread.

Lymphangitis carcinomatosa was so termed by Troisier in 1873. According to a recent series (Harold 1952) it seems to stem most commonly from structures in close proximity to the lung, since the order of frequency in his series is: Bronchus, Stomach, Pancreas, and Breast. In this condition the lymphatic channels throughout the lungs are packed with carcinoma

cells. Radiological visibility depends upon the degree and extent of such a permeation, and the appearance is that of a diffuse reticulation.

In the blood borne miliary carcinomatosis the lungs are incidentally involved as part of a widespread dissemination throughout the body, and groups of carcinoma cells are seen to "pepper" the lungs. If such groups overlap in sufficient intensity in different lung depth-layers, then they are radiologically visible, otherwise their own individual size would not be large enough for radiological definition. (Fig. 1)

Type B Metastases

The type B metastases are small sporadic metastases. They make up the largest group of all, namely 35 per cent of cases.

Although few in number the individual metastases vary in size in the same case, possibly indicating, that they arise from the primary organ at varying intervals of time, some being younger than others. They seem to show a peculiar affinity for the same part of the lung in any one patient. Thus in one case all the metastases would be found in the left lower lobe, whilst in another case solely in the right middle lobe. Only in two did post mortem examination reveal them in both lungs.

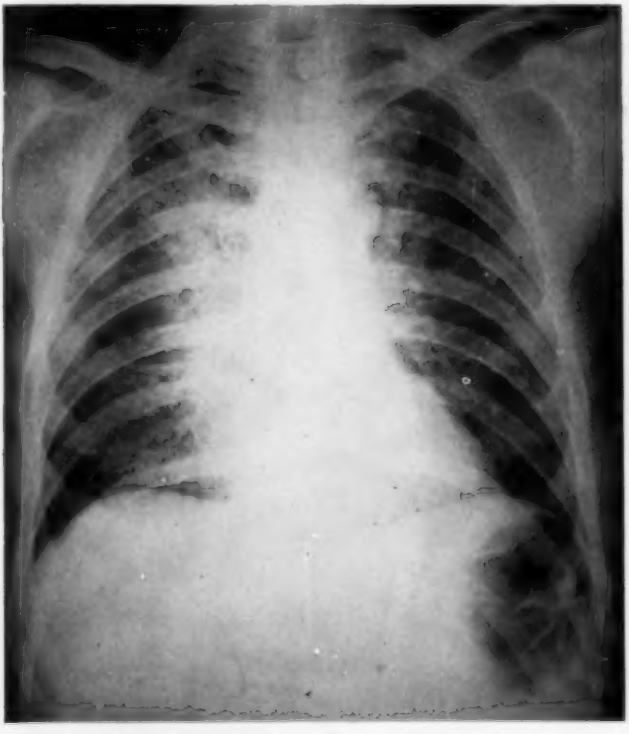

FIGURE 1: Showing miliary carcinomatosis.

Since they were few in number and less than 3 cm. in diameter, they were only apparent radiologically in one-fifth of cases. (Figs. 2*A* and 2*B*)

Type C Metastases

The type C metastases differ from type B in the numbers in which they are present in the lungs. They are the second largest group in this series of cases, representing 30 per cent of them.

They resemble the previous group not only in individual size, but also in that they vary in size in the same patient, metastases being found in the same lung of 1 cm., 1½ cm., 2 cm., and 3 cm. in diameter. This would indicate either that they have different growth rates, or that they are given off at intervals from the primary site as in type B but in larger numbers, rather than in one large outflow, as seems to be the case in the blood borne cases of type A metastases.

The radiological visibility of this type is good, giving radiological opacities in 77 per cent of cases. It is important to compare the ease with which they are radiologically apparent, with the less obvious type B metastases. Although individual metastases are of the same order of size, type C are more numerous. Thus the x-ray beam meets a larger number at different lung-depth layers, and the conditions are more favorable for the production of radiological shadows. (Fig. 3)

Type D Metastases

These are the well-known "cannon-ball tumors." They were radiologically visible in all 14 cases. This is understandable in view of their size. Usually single, few cases showed two or even more similar sized metastases.

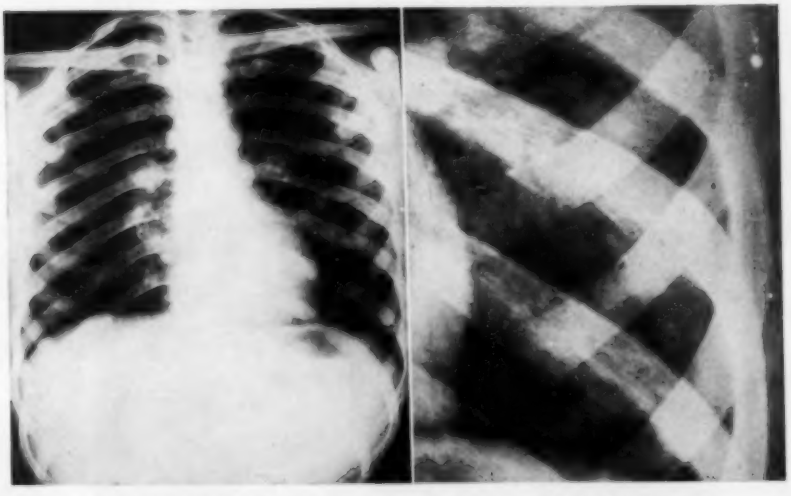

FIGURE 2A FIGURE 2B

Figure 2A: Showing type B metastases in left lower lobe.—*Figure 2B:* Enlargement of left lower lobe.

They do not show affinity for any particular lobe. They could conceivably be type B metastases of low grade malignancy, growing slowly in the lung for some time. They are probably also blood borne.

Cannon-ball tumors are often considered to be characteristic of malignant tumors of the testicle, kidney and prostate. This series does not support this view, since they were found to be secondary to carcinomata of the pharynx (2), colon (1), larynx (1), bronchus (1), breast (1), uterus (1), ovary (1), kidney (2), thyroid (2), suprarenal (1), as well as osteosarcoma (1). (See Table V.) (Fig. 4)

TABLE V

	Post-Mortem Type of the Pulmonary Metastases				
Primary Site	A	B	C	D	E
Mouth and Tongue	—	1	2	—	—
Pharynx	—	—	—	2	—
Esophagus	—	2	—	—	—
Stomach	1	—	—	—	—
Colon	2	2	1	1	—
Rectum	—	3	—	—	—
Liver and Bile Channel	—	3	—	—	—
Pancreas	—	1	—	—	—
Larynx	—	2	—	1	1
Bronchus	3	2	2	1	4
Thymus	—	1	—	—	1
Breast	1	4	6	1	2
Uterus and Cervix	—	2	2	1	—
Ovary	—	1	2	1	—
Prostate	—	—	—	—	1
Testis	—	2	1	—	2
Kidney	1	—	4	2	—
Bladder	—	2	1	—	—
Skin	—	—	1	—	—
Thyroid	—	—	1	2	—
Suprarenal	—	1	1	1	—
Bone	—	1	3	1	1
Lymph and Reticulum	—	4	1	—	—
Fibrosarcoma	—	1	1	—	—
Synoviomata	—	—	1	—	1
TOTAL	8	35	30	14	13

FIGURE 3

Figure 3: Showing type C metastases.—*Figure 4:* Showing a "cannon-ball" tumor.—*Figure 5:* Showing massive replacement of the right lower lobe.

FIGURE 4

FIGURE 5

Type E Metastases

As with type D, this group of 13 cases was also universally demonstrable radiologically, because of their large size. Massive replacement of the lung was frequently the only metastasis, the remaining lung tissue being free of growth. Lower, middle and upper lobes were affected in that order of frequency.

Since they frequently followed excision of the primary neoplasm, it is tempting but debatable to suggest, that a radiologically negative type B metastasis was already present at the time of operation, and the type E occurred by gradual amalgamation of several type B metastases in one lobe.

The organs of the portal system do not seem to give this type of metastasis. When primary bronchial neoplasms produced this metastasis, the secondary growth was distinct, not an extension, of the primary cancer. (Fig. 5)

The Relation of the Grade of Malignancy to Pulmonary Metastases

In an effort to correlate the grade of malignancy of the primary tumor with the frequency of pulmonary metastases the routine pathological reports were consulted, and from these an arbitrary classification into low, medium and high grade of malignancy, according to the histological differentiation was adopted.

This series of cases falls fairly evenly into this grading system (see table VI), indicating that pulmonary metastases are derived equally from low or high grade malignant tumors.

TABLE VI

Grade of Primary	Number of Cases
Low	39
Medium	30
High	31

TABLE VII

	Type of Pulmonary Metastases				
Grade of Primary	A	B	C	D	E
Low	2	20	6	6	5
Medium	4	10	6	5	5
High	2	5	18	3	3

The types A-E are distributed throughout these grades (table VII), and it would be unwarranted to draw conclusions from this distribution, although neoplasms of low grade malignancy are more apt to produce type B metastases, and those of high grade to produce type C metastases.

Conclusions Regarding Radiological Evidence

Metastases were not radiologically "visible" and so were missed in nearly 40 per cent of this series of pulmonary metastases, an unsatisfactory state of affairs in the assessment of any carcinoma patient.

One of the important factors in producing radiological shadows is a product of the size and numbers of metastases. When metastases were few and less than 3 cm. in diameter, they were frequently missed, whereas those of similar size, if numerous, were well seen in chest x-ray films. Those greater than 3 cm. in diameter were radiologically obvious even when single.

SUMMARY

1. One hundred autopsy confirmed cases of pulmonary carcinomatosis were analyzed, and correlated with the presence of metastases radiologically.

2. It was found that nearly 22 per cent of cancer cases had pulmonary metastases. The relative frequency of primary neoplasms producing such metastases is outlined, and their modes of spread (portal and systemic) compared.

3. The metastases were divided into five types according to their size and density. The product of their size and density was stressed as an important factor in radiological visualization.

4. The primary tumors comprising the series were graded according to their degree of malignancy and correlated with the frequency of pulmonary metastases.

5. Conclusions based on the radiological evidence were then discussed.

RESUMEN

1. Se llevó a cabo un análisis de 100 casos de carcinomatosis pulmonar confirmada a la autopsia y se correlacionaron con la presencia de metástasis radiológicamente.

2. Se encontró que aproximadamente 22 por ciento de los casos de cáncer tenían metástasis pulmonares. La frecuencia relativa de los neoplasmas primarios que producen tales metástasis se describe así como sus modos de propagación (portal y general) se comparan.

3. Las metástasis se dividen en cinco tipos de acuerdo con su tamaño y densidad. El producto de su tamaño y densidad se recalca como un factor importante para su visualización radiológica.

4. Los tumores primarios que comprenden estas series se escalonaron de acuerdo con su grado de malignidad y se correlacionaron según la frecuencia con que hicieron metástasis pulmonares.

5. Se llegó entonces a la discusión de las conclusiones basadas en la evidencia radiológica.

RESUME

1. Cent autopsies de cancers pulmonaires certains ont été étudiées en fonction de la présence de métastases radiologiques.

2. L'auteur constata que près de 22% des cancers avaient été à l'origine de métastases pulmonaires. Il précise la fréquence relative de cancers primaires produisant de telles métastases et compare leurs modes d'extension.

3. Les métastases furent réparties en cinq groupes, selon leur dimension et leur densité. L'auteur insiste sur l'importance pour leur mise en

évidence radiologique de la combinaison de leur taille et de leur densité.

4. Les tumeurs primaires dans les cas étudiés furent classées selon leur degré de malignité et en fonction de la fréquence des métastases pulmonaires.

5. L'auteur a exposé ensuite ses conclusions fondées sur les constatations radiologiques.

ZUSAMMENFASSUNG

1. Es wurden 100 autoptisch bestätigte Fälle von pulmonaler Carcinomatose analysiert und in Beziehung gesetzt zu dem radiologischen Vorhandensein von Metastasen.

2. Es fand sich, dass nahezu 22% der Krebsfälle pulmonale Metastasen aufwiesen. Die relative Häufigkeit von primären, solche Metastasen bildenden Neoplasmen wird skizziert und ihre Ausbreitungsart verglichen (Im Pfortader—und im Körper-Kreislauf).

3. Die Metastasen wurden in 5 Typen eingeteilt, entsprechend ihrer Grösse und Dichte. Das Ergebnis aus ihrer Grösse und Dichte wurde als ein wichtiger Faktor in der radiologischen Darstellbarkeit herausgestellt.

4. Die primären Tumoren, aus denen die Reihe besteht, wurden eingeteilt entsprechend ihrem Grad von Bösartigkeit und in Beziehung gesetzt zur Häufigkeit pulmonaler Metastasen.

5. Besprechung der auf dem radiologischen Zeugnis basierenden Schlussfolgerungen.

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Case Report Section

Three Cases of Circumscribed Pulmonary Opacities Simulating Tumor

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It is now 35 years since the report of the Framingham Demonstration by the National Tuberculosis Association[13] and 60 years since the discovery of Roentgen rays. In the intervening period there has been a vast increase in the use of routine chest radiography and mass population x-ray surveys. In consequence, clinicians have been confronted more and more with the problem presented by the diagnosis and treatment of circumscribed pulmonary radiodensities, often called "coin lesions."

Though lesions of this type had previously been noted, it was not until relatively recently that thoracic surgery, with the impetus of improved techniques and accumulated experience, better anesthesia and the aid of antibiotics, has become a feasible procedure for the routine investigation of undiagnosed pulmonary disease. In 1936 Graham and Singer[6] reported the resection of pulmonary lesions simulating tumor. They found them to be tuberculomas. Alexander[1] in 1942 called attention to the problem of intrathoracic neoplasms. Subsequently, an extensive literature has appeared on the subject.

Among these lesions there are always found a number of tumors which are indistinguishable from the benign densities except by histological examination. Surgical excision, therefore, has been repeatedly advocated as the only safe therapy. The pertinent question has become, not whether a lesion of this type should be resected, but whether it is capable of complete removal.

The procedure to be followed in the period between the finding of the radiographic abnormality and the point at which thoracotomy is performed has received relatively little attention. This, in spite of the large percentage of inflammatory, granulomatous and cystic opacities exclusive of tuberculomas, reported in some large series. Overholt[10] found 26 per cent (52 in 200 cases), including a large number of shadows due to bronchiectasis (Table I). Abeles and Ehrlich[2] encountered 19 per cent (4 in 21 cases), while Davis and Klepser observed 11 per cent (8 in 71 cases). Storey et al,[11] on the other hand, found only a xanthogranuloma and one coccidioma in 67 cases, both of which are relatively unchangeable and require excision for diagnosis. Findings of other authors have fallen somewhere between these latitudes (Table I). Effler, Blades and Marks[4] find no inflammatory lesions in young service personnel but a high incidence of tuberculomas and 29 per cent cysts (7 in 24 cases). Flavell[5] tells of a small abscess

From the Medical Service, Veterans Administration Hospital.

simulating a tumor, but which later developed a fluid level and vanished after antibiotic therapy.

The cases here reported were believed at the time of admission to have pulmonary tumors because of the finding on the x-ray film of circumscribed radio-opacities. However, each patient underwent the usual diagnostic study and evaluation and received therapy for the associated conditions. Subsequently it was noted that the shadows thought to be neoplastic, had changed or disappeared. This resulted in a marked alteration in the clinical outlook and prognosis in these patients.

An awareness of the existence of lesions of this type should aid in the

TABLE I*

Author	Total Cases	Tumors Malignant No.	Per Cent	Tumors Benign No.	Per Cent	Tuberculoma No.	Per Cent	Cystic, Granulomatous** Inflammatory No.	Per Cent
Overholt (1951)	200	60	30	10	5	63	31.5	52	26
Hood, Good, Clagett, McDonald (1948)	156	55	35	30	19	65	42	6	4
Davis and Klepser (1950)	71	37	52	9	13	17	24	8	11
Storey, Grant, Rothman (1953)	40	7	17.5	2	5	28	70	2	5
Effler, Blades, Marks (1948)	24	4	17	2	8	8	33	7	29
Abeles and Ehrlich (1951)	21	8	38	3	14	5	24	4	19
O'Brien, Tuttle, Ferkaney (1948)	21	9	42	1	5	8	38	3	14

*Miscellaneous, undetermined and other categories were used in the computation of the percentages but are not included in the table.
**Exclusive of tuberculomas.

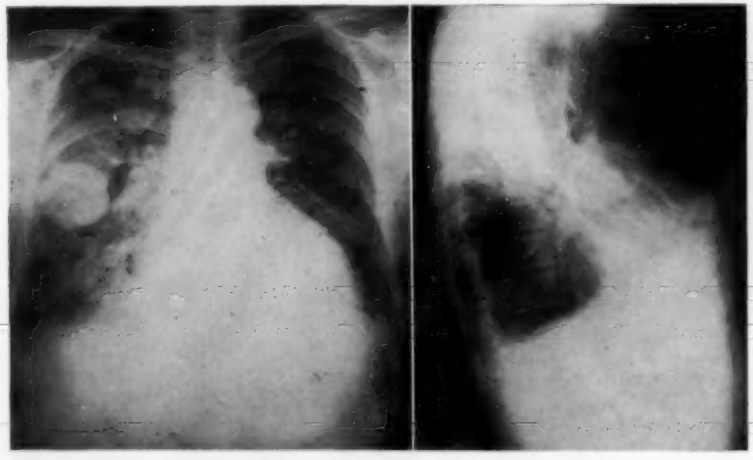

FIGURE 1 (CASE 1): Posterior-anterior and lateral views of the chest taken June 24, 1954, show a rounded circumscribed opacity in the right mid-lung thought to be tumor. Posterior to this is a fusiform density representing an interlobar effusion. Inferiorly a triangular shadow is seen on the lateral view which was thought to be atelectasis.

discovery of others. Until better methods are available, each patient with circumscribed pulmonary opacities should be evaluated with a view to rapid surgical exploration. A thorough routine presurgical study will usually separate those with benign conditions from the cases which require thoracotomy.

Case 1: This 59 year old white male janitor entered the Portland Veterans Administration Hospital on November 26, 1954 complaining of shortness of breath. He had known of having hypertension for about one year, recalling that his systolic blood pressure in December, 1953 was 220. Following a hernioplasty in April, 1954, he had been relatively well until July, when he began to notice exertional dyspnea. Soon after, he developed orthopnea and spent several nights sitting on the edge of the bed because

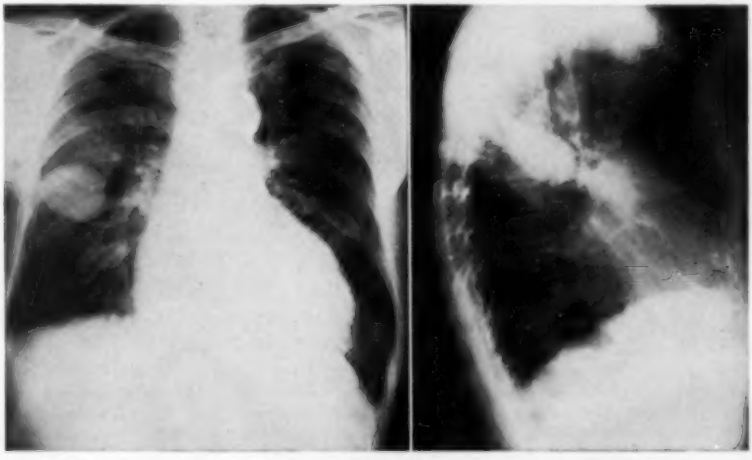

FIGURE 2 (CASE 1): Posterior-anterior and lateral chest films taken about two weeks following admission show a change in both the size and shape of the rounded, circumscribed density and the posterior fusiform shadow. The lower triangular shadow is now absent.

FIGURE 3 (CASE 1): Posterior-anterior and lateral views taken three weeks after admission show the disappearance of all but the posterior fusiform density.

of a feeling of suffocation. These symptoms were progressive in severity. In addition, a substernal sensation of pressure developed which was precipitated by exertion and relieved by rest. He sought the advice of a physician on November 20, 1954. A chest x-ray film was taken and because of the finding of a large solitary circumscribed density in the right mid-chest he was referred to the hospital.

It was found at that time that he had had cough for about four weeks productive of up to one hundred ml. of mucoid sputum daily. He had noted occasional blood tinging. Also, he recalled having had two episodes of gross hematuria in July, 1954. None had occurred before or since.

Physical examination revealed an irritable, pale white male of asthenic build, slightly dyspneic at rest. The temperature was normal, pulse 90 and regular and the blood pressure was 238/138. Significant findings included flame shaped hemorrhages in the fundi, copper wiring of the arterioles and papilledema. The chest expanded well and equally on both sides and was resonant to percussion throughout. Breath sounds were normal except in the upper half of the right chest anteriorly where there was a decrease in the intensity of transmission. Over the base of the right lung laterally, there were heard a few crepitant rales. The cardiac apical impulse was palpable in the sixth intercostal space in the anterior axillary line and was forceful. At the cardiac apex a loud, low pitched murmur was present and transmitted into the axilla. Over the right second intercostal space parasternally a soft high pitched murmur was heard, and it was transmitted into the neck. The aortic second sound was increased in intensity and louder than the second pulmonic sound. The remainder of the physical examination was unremarkable.

Laboratory studies included hemoglobin 11.6 grams, red blood cell count 3.67 million, and white cell count 7200 with normal differential count. Urinalysis revealed albuminuria varying from one to two plus and ranged in specific gravity from 1.005 to 1.010. Formed elements included 3-4 rbc/HPF and 5-10 wbc/HPF as well as occasional hyaline and granular casts. Blood serology was negative and the blood urea nitrogen was 45.5 mgm. per cent.

A posterio-anterior x-ray film of the chest had been taken March 1, 1954 and showed moderate cardiac enlargement and obliteration of the right costophrenic angle, but no parenchymal infiltration. At the time of admission to the hospital a posterio-anterior x-ray film showed considerable cardiac enlargement and a six centimeter circular density in the fourth intercostal space anteriorly on the right (Fig. 1). A lateral view indicated the opacity to be in the mid chest anterior to the hilum. A fusiform, density was present in the right upper chest in the area of the interlobar fissure, posterior to the hilum. In the right lower chest was a triangular density with its apex in the hilum and extending downward adjacent to the heart.

Because of signs and symptoms of congestive heart failure and the presence of elevated venous pressure and circulation time, he was digitalized and given a low

FIGURE 4

FIGURE 5

Figure 4 (CASE 2): Posterior-anterior view film taken on August 1, 1953, demonstrates a rounded opacity just lateral to the left cardiac border at the eleventh posterior rib.—*Figure 5* (CASE 2): Follow-up chest film taken May 12, 1954, illustrates the disappearance of the density present ten months previously.

salt diet. Subsequent chest x-ray films indicated first a decrease in the size and a change in the shape of the rounded density, then its complete disappearance. The fusiform density in the upper chest also decreased in size but did not entirely regress (Figs. 2 and 3).

Case 2: This 58 year old white male farmer was admitted on August 18, 1953 to the Portland Veterans Administration Hospital because of easy fatigability, and chronic cough productive of mucopurulent sputum for about two years. Previously he had been in good general health.

At the time of admission temperature, pulse and respiration had been normal. Blood pressure was within normal range. Significant findings included slight increase in the AP diameter of the chest. It was symmetrical and normal respiratory movements were observed bilaterally. The breath sounds were vesicular throughout and the percussion note was normal. No evidence of consolidation or fluid was obtained. However, crepitant rales were heard over the left chest anteriorly and laterally at the margin of the left cardiac border. The remainder of the physical examination was unremarkable.

Laboratory reports indicated a normal hemogram with white cell count of 7800 and normal differential count. No abnormality was found in the urine and the blood serology was negative. The blood urea nitrogen was 14.7 mgm. per cent. A first strength intradermal tuberculin test was faintly positive but coccidioidin and histoplasmin skin tests were negative. Sputum cultures were negative for acid fast bacilli.

At the time of admission a posterio-anterior x-ray film of the chest showed the presence of a rounded radiodensity on the left just lateral to the cardiac silhouette (Fig. 4).

He was put to bed and instructed in postural drainage because he was expectorating one cup of mucopurulent sputum daily. He remained afebrile throughout the hospital stay and, in view of the normal white cell count, no antibiotic therapy was given.

Bronchography, bronchoscopy and surgery were under consideration when a repeat chest film revealed a decrease in the size of the radio-opacity, which subsequently disappeared (Fig. 5).

The patient was discharged asymptomatic three weeks following admission.

Case 3: This 30 year old white male logger was first admitted to the Portland Veterans Administration Hospital on July 14, 1953 because of shortness of breath and a "mass in the lung."

He believed that he had had rheumatic fever with joint pains at the age of seven years, but he knew of no heart disease. Following the acute illness he felt well and was under no limitations insofar as physical activity was concerned.

In 1945 while in the army he noted the onset of joint pains and swelling and was hospitalized. He was told that he had rheumatic fever and one of the valves in the

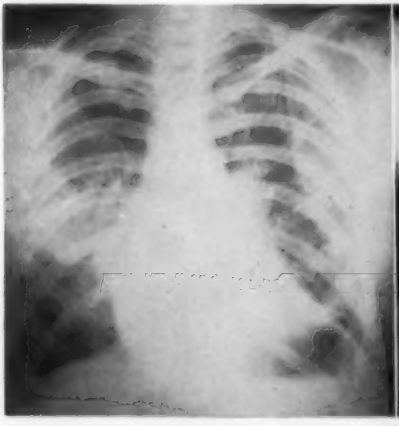

FIGURE 6

FIGURE 7

Figure 6 (CASE 3): Posterior-anterior view of the chest at the time of admission show a rounded, circumscribed opacity in the right mid-chest.—*Figure 7* (CASE 3): Posterior-anterior view of the chest taken on December 15, 1954, three months following admission, indicates a loss of the rounded opacity.

heart was leaking. He was discharged from the armed forces because of this disability.

He returned to his home in Oregon and worked as a logger until 1952, a year prior to admission. At that time he had to discontinue work because of shortness of breath and tightness in the chest. After exertion he noted an exacerbation of his cough with occasional production of blood tinged sputum. He lost 20 pounds during this period.

He sought advice from his personal physician who took a chest x-ray film. A large, rounded radiodensity was seen in the right mid-chest and this was thought to represent a tumor mass for which he should be hospitalized.

Physical examination at the time of admission revealed a white male who did not appear to be acutely ill and who had a normal pulse, blood pressure and temperature. Respirations were not rapid. Significant findings included a symmetrical chest with no observable abnormalities except for a prominent apex beat 9 cm. to the left of the midsternal linc in the sixth intercostal space. Percussion and fremitus were normal but auscultation revealed sibilant rales throughout both lung fields and crepitant rales at both pulmonary bases posteriorly. A rough, loud presystolic murmur and a low amplitude, medium pitched systolic murmur were heard in the area of the cardiac apex. In addition, a high pitched, soft diastolic murmur was present over the right second intercostal space parasternally and it was heard transmitted down the left side of the sternum. No other significant physical finding was observed.

Laboratory reports indicated a normal hemogram and urinalysis. The serology was negative and the blood urea nitrogen 14.0 mgm. per cent.

Chest x-ray film at the time of admission revealed the presence of a rounded, circumscribed opacity in the right mid-lung field (Fig. 6). It was thought that he had rheumatic heart disease, inactive with mitral stenosis, mild mitral valve insufficiency and slight aortic valvular insufficiency. The venous pressure and circulation time were found to be elevated and digitalization was accomplished. At the same time, because of cough and expectoration of mucopurulent sputum penicillin was given intramuscularly.

Subsequent chest films showed the disappearance of the rounded infiltrate in the mid-chest. In its place were seen persistent band-like densities thought to be due to pleural thickening (Fig. 7). Shortly thereafter he underwent mitral commissurotomy and was subsequently discharged improved.

Discussion

Three cases are presented in which circumscribed, rounded radiodensities were observed in the admission chest film. In Case 1 the x-ray film was interpreted as showing a solitary spherical mass in the right mid-lung field with atelectasis of the right middle lobe and an interlobar effusion between the lower and upper lobes posterior to the hilum. Because of the history of hematuria and the circumscribed pulmonary opacity it was thought that he had a pulmonary tumor, likely metastatic from the kidney. Cardiovascular disease and the existence of hypertension were also recognized. Therefore, digitalis, a low salt diet and bed rest were instituted. Subsequent chest films first revealed a decrease in the size of the rounded opacity (Figure 2), then its complete disappearance (Figure 3). It became evident that the shadow was not due to tumor, but more likely to an interlobar effusion caused by congestive heart failure.

An admission chest x-ray film showed a rounded density just to the left of the cardiac silhouette in Case 2. This was thought possibly to represent a tumor. Because he was expectorating much sputum, he was instructed in postural drainage but no specific medication or antibiotic was given. In the meantime a thorough presurgical evaluation was planned. Repeat x-ray films first indicated a marked diminution in size, then the absence of the density (Figures 4 and 5). This was then thought to be due to an inflammatory process associated with chronic bronchitis or bronchiectasis.

Case 3 was admitted because of cough, blood streaked sputum and the

presence of a rounded density in the right mid-lung field which was thought to be a tumor mass. Physical examination promptly revealed the presence of rheumatic heart disease. Evidence for congestive heart failure was discovered and digitalis and bed rest were instituted. The circumscribed shadow in the right chest was still thought to be a separate process. However, subsequent films revealed its regression and disappearance. It was then considered to be pleural effusion, though an inflammatory condition cannot be eliminated, inasmuch as penicillin was also given.

In each case the admission diagnosis was pulmonary tumor. Though the prognosis seemed poor, thorough routine clinical studies were carried out and therapy was instituted. The outlook changed in the three cases. The first is still in the hospital, but his cardiac insufficiency is under effective treatment and he should soon expect discharge. Case 2 left the hospital three weeks after admission and remains in good general health though there are frequent respiratory infections. Case 3 underwent mitral commissurotomy following which he was discharged improved.

Cases of this type should have repeated chest films, including laterals and obliques when the nature of the lesion is not well defined; in addition, a detailed history, a complete physical examination, hemogram, urinalysis, blood urea nitrogen or nonprotein nitrogen should be obtained. Other studies will be required depending upon the characteristics of the individual case. Bronchoscopy and bronchography are often helpful.

Early thoracotomy, usually not later than two to three weeks after admission, should follow a thorough evaluation unless the patient is considered inoperable.

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Simultaneous Hypersensitivity to Streptomycin and Para-Aminosalicylic Acid

REPORT OF TWO CASES

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Drug hypersensitivity implies an unpredictable reaction, not related to dosage, with allergic manifestations, based upon an immune mechanism.[1] There have been a number of reports of such reactions to either streptomycin[2] or para-aminosalicylic acid,[1, 3, 4, 5] but the number of reports of combined hypersensitivity to both drugs are few.[6, 7, 8] The occurrence at the same time in one hospital of two instances in which patients reacted unfavorably to both streptomycin and para-aminosalicylic acid is believed to be sufficiently unusual and interesting to justify report.

Manifestations of hypersensitivity to either or both of these drugs vary from rash and fever to states simulating infectious mononucleosis,[4, 5] hepatitis,[5, 6, 9] central nervous system disease,[10] exfoliative dermatitis, and even death.[11] The following case reports illustrate the serious nature of these reactions and the problems encountered in their management.

Report of Cases

Case 1: D. L. G., a 20 year old Caucasian man, was admitted to the hospital on May 19, 1954, complaining of pain in the right chest of about two weeks duration. Five months previously he had failed to react to 0.0001 mgm. of Purified Protein Derivative. A history of allergy in his family (seasonal asthma in his mother and wheat dust reactivity in his father) was elicited.

Physical examination on admission revealed a temperature of 100° F. and evidence of pneumonitis in the right lower chest. Routine blood and urine studies were not remarkable except for sedimentation rate of 22 mm./hr. Roentgenogram of the chest suggested at first early consolidation in right lower lobe. By May 28, 1954, however, frank right pleural effusion was apparent, and thoracentesis on June 1 and 4, 1954, yielded a total of two liters of amber fluid, rich in lymphocytes, but negative for M. tuberculosis on smear and culture. Cultures of the fasting gastric content and of the sputum, made at this time, were later reported to contain that organism. On clinical grounds, primarily because the tuberculin reaction had now become positive, the diagnosis pleurisy tuberculous with effusion was established, and on June 16, 1954, treatment with streptomycin (1.0 g. twice a week) and para-aminosalicylic acid (12.0 g. daily) was initiated. The patient's immediate response, both subjective and objective, was gratifying.

On July 12, 1954, 26 days after the start of chemotherapy, he did not feel well and his temperature was 100° F. On July 14, 1954, a diffuse morbilliform irruption was noted on the skin. Since unfavorable response to medication was suspected, both chemotherapeutic agents were stopped, and an anti-histaminic drug was employed. The dermatosis, however, proceeded to exfoliation, generalized, tender lymphglandular enlargement and hepato-splenomegaly appeared, and his condition became critical. The blood contained 18,900 leucocytes per cubic millimeter, of which 43 per cent were lymphocytes and 16 per cent eosinophiles. Toxic granulation of the neutrophiles was reported, and many of the lymphocytes were said to be abnormal. On July 18, 1954,

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The opinions or assertions contained herein are private ones of the writers and are not to be construed to be official or reflecting the view of the Navy Department or the Naval Service at large.

the daily administration of ACTH (40 mgm.) by intravenous drip was begun.

On July 23, he complained of swelling about the eyes, abdominal distension, and bilateral aching in the loins. He became oliguric, and the dilute urine contained albumin, erythrocytes, and casts. Blood urea nitrogen was found to be 56.6 mgm. per hundred cc. Because of manifest fluid and nitrogen retention, fluid and salt intake was limited and ACTH gel (40 mgm.) was given daily intramuscularly in place of the intravenous dose. Diuresis ensued, with loss of 13 pounds of body weight in five days. The dosage of ACTH was gradually decreased and was finally discontinued on August 6, 1954, by which time the skin had cleared.

As the skin improved, profound serologic alterations were noted, namely hypoalbuminemia (3.25 g. per hundred cc.), hyperglobulinemia (4.5 g. per hundred cc.), cold agglutinin titer of 1:64, and heterophile presumptive titer of 1:112. Leucocytosis reached 26,900 cells per cubic millimeter, with a maximum eosinophilia of 27 per cent. Mild hepatic dysfunction was evidenced by thymol turbidity test (6 units) and the prothrombin time (60 per cent of normal), but neither clinical nor serological jaundice appeared.

By August 10, 1954, about one month after the onset of the reaction, blood and urine components approached normal, although the blood urea nitrogen and globulin remained elevated. The kidneys concentrated and diluted the urine satisfactorily, but 12-hour urine sediment continued to show an excessive number of leucocytes, erythrocytes, and casts. Investigation of the kidneys by intravenous pyelography revealed no anatomical defect, and M. tuberculosis was not recovered in the urine.

In the belief that the unfavorable reaction had been due to para-aminosalicylic acid, on August 10, 1954, streptomycin (0.25 g.) and isoniazid (300 mgm.) were administered. Within 12 hours a macular dermatosis appeared and an eosinophilia of 34 per cent. Medication was discontinued, and the skin cleared within one week.

On September 2, 1954, a test dose of para-aminosalicylic acid (0.5 g.) produced a pruritic eruption, papular in nature, with fever which lasted three days. The leucocyte count rose to 13,000 cells per milliliter cubed, and the eosinophiles to 16 per cent.

In view of the fact that the patient was about to be transferred to a Veteran Administration Facility, no attempt was made to desensitize him. At the time of transfer he appeared to be well. It was learned subsequently, through the courtesy of the Veterans Administration Hospital, Albuquerque, N. M., that he left against medical advice on October 4, 1954, and there is no further information available as to his subsequent course.

Case 2: R. R. N., a 41 year old Negro man, was admitted to the hospital on August 13, 1954, with far advanced, active, pulmonary tuberculosis, detected by a routine chest roentgenogram, and bacteriologically proved. Chemotherapy with streptomycin (1.0 g. twice a week) and para-aminosalicylic acid (12 grams daily) had already been instituted at another hospital.

Admission pnysical and roentgenographic examinations revealed widespread disease in both upper lobes, with bilateral exudation and cavitation. Smears of the sputum contained acid-fast bacilli. The erythrocyte sedimentation rate was 19 mm./hr., and the blood contained 5700 leucocytes per cubic millimeter, 53 per cent of which were polymorphonuclear leucocytes, 41 per cent lymphocytes, and 3 per cent eosinophiles. Urinalysis and blood Kahn reaction were not abnormal.

On August 22, 1954, 41 days after the start of chemotherapy, he complained of a sore throat, and examination revealed a reddened pharynx. The temperature was 104° F. Procaine-penicillin (600,000 units daily) was prescribed for a supposed intercurrent pharyngitis. The temperature, however, remained elevated, and two days later he complained of headache and appeared to be lethargic. The urine was albuminous and contained casts, the leucocyte count was 30,000 per cubic millimeter, with 84 per cent polymorphonuclear cells, and a sample of the spinal fluid, withdrawn because the possibility of meningitis was entertained, contained 26 cells per cubic millimeter, all lymphocytes. Because of this finding, isoniazid (600 mgm. daily) was added. Later, however, the appearance of generalized lymphglandular enlargement, generalized, confluent, macular irruption on the skin, and eosiniphilia of 9 per cent pointed to drug intolerance as the most plausible explanation of the acute illness, and on August 25, 1954, streptomycin and para-aminosalicylic acid were stopped. Isoniazid, which did not appear to be incriminated, was continued.

By August 26, 1954, the temperature had fallen to 102° F., but exfoliation of the skin set in and the blood eosinophilia continued to rise, reaching a maximum of 26 per cent. Thereafter, fever remained in abeyance, and by September 10, 1954, lymphglandular enlargement and eosinophilia had receded, and the dermatosis was improving.

Since streptomycin was considered to be the offending agent, on September 24, 1954, he was given a test dose of para-aminosalicylic acid (3.0 g.). Within three hours fever, shaking chills, and an eosinophilia of 25 per cent occurred.

On October 6, 1954, he tolerated 0.1 gram of streptomycin without difficulty, but a dose of 0.5 gram administered next day was followed by fever, chills, and eosinophilia of 24 per cent within three hours.

Because it was apparent that he reacted unfavorably to both drugs, isoniazid was continued in doses of 300 mgm. daily and desensitization to para-aminosalicylic acid by the method of Hayes and Weiss[1] was begun and successfully carried to completion. Eight months later, when last seen he was taking both isoniazid and para-aminosalicylic acid in usual dosage without ill effect and with excellent results as far as his tuberculosis was concerned.

COMMENT

The reproduction of reactions to both streptomycin and to para-aminosalicylic acid in each of these patients separately indicates that they were hypersensitive to both drugs. Whether the hypersensitivity to one of the drugs prepared the way for hypersensitivity to the other, or whether each of these individuals was independently hypersensitive to both agents we do not know. We suspect that the former was the case. Nevertheless, as a practical matter simultaneous hypersensitivity was a fact.

Both patients presented the following manifestations of hypersensitivity: fever, leucocytosis, eosinophilia, exfoliative dermatitis, generalized lymph-glandular enlargement, and toxic nephritis. In addition, Case 1 showed evidence of abnormal lymphocyte formation, hepato-splenomegaly, and serologic alterations. Case 2 had symptoms suggesting meningitis and a pleocytosis in his spinal fluid.

The use of ACTH in Case 1 is believed to have been life-saving.[12, 13]

The usefulness of isoniazid as an available alternative chemotherapeutic agent against tuberculosis is obvious, as is also the usefulness of a practical method of desensitization to para-aminosalicylic acid.

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Co-existence of Bronchial Adenoma with Pulmonary Tuberculosis

A CASE REPORT

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In the past 20 years, there has been an increasing amount of information forwarded regarding the tumor generally known as bronchial adenoma. Much has been said regarding their classification and nomenclature. Out of many names, those of cylindroma and carcinoid emerge as those in common usage to denote histologic types of bronchial adenoma. There are those who would stress the differences between the two types as being more than based on differences of histologic appearance. Enterline and Schoenberg[1] point out that cylindroma causes death or tends to recur seven times as frequently as the carcinoid type. They also feel that cylindroma occurring in the tracheobronchial tree is identical with those tumors arising from salivary glands and ducts, paranasal sinuses and palate, and when occurring in these sites, they are called carcinoma. On the other hand, Davey and Hardy[2] feel that cylindroma only superficially resembles the above-mentioned tumors in the salivary glands, paranasal sinuses and palate, and, that certain histologic changes that do occur in them, are not present in cylindroma. For the purpose of this report, it is our belief that Doty's[3] point of view is the most practical. That is, it is of little practical importance to stress the difference in these two types of this tracheobronchial tumor, since each type gives the same clinical picture, each can be locally invasive and even distantly metastasizing, thereby necessitating the same therapeutic approach.

What is generally agreed upon is that it is more common in women than in men, and that in at least 50 per cent of the cases, it occurs in patients below thirty years of age. It is slow-growing. The duration of symptoms before a diagnosis was made in a series analyzed by Herbut[4] was from two to eight years. Moersch and Harrington,[5] in a summary point out that symptoms produced depend on the location, size of the tumor, and the characteristically easy bleeding of these tumors. Thus, they are marked clinically by hemoptysis, and the sequelae to bronchial irritation and obstruction, i.e., cough, wheezing (usually unilateral), fever, chest pain and dyspnea. Fifteen per cent of a series of 100 cases quoted by Moersch and Harrington had no pulmonary symptom, presumably because they did not cause obstruction or interfere with drainage of the bronchus. Chest x-ray findings are usually those of atelectasis, though occasionally a well-delineated, round density is seen.

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When faced with a clinical picture and chest x-ray film appearance conforming with the above, the differential diagnosis would consist mainly of eliminating bronchiogenic carcinoma or tuberculosis. Obviously, other diseases might be considered, but these two would probably remain uppermost in the diagnostic approach. The age and sex characteristics of the patient, and the duration of symptoms, may be of some aid in the differentiation of bronchial adenoma from bronchiogenic carcinoma. The fact that in two-thirds of cases of bronchial adenoma the tumor involves the main lower lobe bronchi, while lower lobe tuberculosis as the initial or sole site is relatively uncommon may be helpful in differentiating this tumor from tuberculosis. Bronchoscopy would be of greatest aid at this point, for, if a tumor were found, it could be biopsied. In the face of sepsis, however, especially in a young woman with the presence or history of hemoptysis, it is conceivable that one might hesitate before bronchoscopy in order to institute a search for acid-fast bacilli in the sputum. If this yielded no tubercle bacilli, then, probably, bronchoscopy would follow. On the other hand, if acid-fast bacilli were found in the sputum, the temptation would be present to explain the clinical picture entirely on the basis of active, pulmonary tuberculosis. One reason for this report is to emphasize the fact that to yield to the above temptation, especially in the face of atelectatic-appearing, lower lobe disease, would be a serious oversight.

The other reason for this report is that a review of the literature pertaining to bronchial adenoma fails to reveal mention of this tumor existing in conjunction with proved pulmonary tuberculosis, except for a report by Zorini.[6] He describes a patient who received the diagnosis of pulmonary

FIGURE 1

tuberculosis on clinical grounds alone, without bacteriologic confirmation, and who was placed in a sanatorium. He continued to have negative sputa for several years, before finally developing actual tuberculosis because, in Zorini's opinion, of his exposure to the disease in the hospital. The patient was later found to have bronchial adenoma.

In a clinicopathologic exercise in an issue of the *New England Journal of Medicine* of 1953, the patient discussed had a history of over 30 years of intermittent hemoptysis. Before the true nature of her condition was finally ascertained, she had been treated for pulmonary tuberculosis, the diagnosis having been made clinically and without bacteriologic confirmation. Following operation for bronchial adenoma after the diagnosis had finally been made, histologic examination failed to reveal evidence of tuberculosis. Aside from the above two, the articles already referred to in this report, in addition to review articles by Delarue[8] and McBurney,[9] fail to document cases of tuberculosis of the lung co-existing with bronchial adenoma.

E. G., a 25 year old negress, entered Philadelphia General Hospital on May 1, 1953, with the chief complaint of easy fatigue of two months duration. She had been in this hospital in 1945, 1946 and 1948 for uneventful deliveries of infants. On the last of these admissions, a chest x-ray survey film was taken and was read as, "Increased markings, both bases." She failed to return for x-ray film follow-up until March of 1949, when a well-delineated density was seen in the right lower lung field, adjacent to the heart shadow. She was referred to the City Chest Clinic of her district, but did not comply with this recommendation, and was lost from observation.

One year prior to the admission of May 1, 1953, she had an episode of hemoptysis. She did not seek medical attention until four months prior to admission, when she went to the outpatient clinic of another hospital for pre-natal care. The previously described lesion was noted by chest x-ray film. Smears of sputum were found to be positive for acid-fast bacilli, and she was sent to Philadelphia General Hospital for admission to the tuberculosis department.

On admission, physical examination revealed blood pressure of 105/60, respirations of 20/min., pulse of 80/min. and normal temperature. The other positive findings were: coarse rhonchi in the base of the right lung posteriorly; the abdomen enlarged with a symmetrical mass compatible with a five month pregnancy; several small, firm, shotty nodes in both inguinal regions. The admission chest x-ray film was read as follows: "The left lung field is normal, with deviation of the heart and mediastinum to the right. The right diaphragm is elevated. There is a homogeneous density, sharply circumscribed, in the right base, measuring 5 by 6 cm. in diameter. It is adjacent to the right cardiac border." (Fig. 1).

A culture for acid-fast bacilli from sputum was positive. Because of the localized physical findings in the chest, and of the atelectatic appearance of the lesion, bronchoscopy was done. It was found that the right middle lobe orifice was blocked by "granulation tissue." Biopsy report stated: "Specimen consists of fragments of connective tissue containing cords and nests of epithelial cells surrounding cylindrical masses of hyaline material. There are no mitotic figures. There is no evidence of tuberculosis. Impression: probably adenoma (cylindroma) of the Bronchus." It was decided to continue treatment, consisting of streptomycin and PAS, and wait until obstetrical delivery. She was delivered of a normal infant on Sept. 28, 1953 and had an uneventful post-partum period.

Thoracotomy was done on Oct. 28, 1953. The description of the findings seen at surgery follows: "There was a large, rounded mass about 3-4 cm. in diameter involving most all of the hilar structures. It appeared to be surrounded by inflammatory tissue. It directly invaded the pericardium at one point. The entire middle lobe, distal to the tumor, was atelectatic. The pleural cavity was normal. Right pneumonectomy was performed, and a section of pericardium was removed with the hilar tumor. Post-operative dissection of the removed lung revealed the tumor arising from the middle lobe bronchus."

The report of the gross and histologic examination states, "The specimen consists of the right lung with a pinkish, firm mass, 4 cm. in diameter, and a small white mass, both lying on the medial surface of the lower lobe. The tumor appears to be encapsulated. Microscopic sections reveal cords of clear, polygonal cells which are not anaplastic. The stroma is formed of loose, edematous connective tissue with strands

of fibrillar eosinophilic material resembling those seen in cylindroma." Additional sections were taken from the surrounding inflammatory tissue and revealed that, "Throughout the tissue there are tubercles composed of foci of caseation necrosis surrounded by lymphocytes, plasma cells, epithelioid cells, Langhans giant cells and fibroblasts. Acid-fast stain reveals the presence of acid-fast rods within some of the caseous lesions. Pathologic diagnosis: 1. Bronchial adenoma. 2. Pulmonary tuberculosis."

Discussion

Zorini's patient,[6] could have been spared a great deal of difficulty had bronchoscopy been done early. In the case presented by us, it is noteworthy that bronchoscopy was done in spite of finding tubercle bacilli in the sputum, which had apparently completely satisfied the referring hospital as to the exclusively tuberculous etiology of the findings. It is felt that this underscores the usefulness of routine bronchoscopic examination as part of the evaluation of almost all patients with pulmonary tuberculosis.

This report points out that bronchial adenoma and pulmonary tuberculosis may occur together, though apparently not often, and they do not mutually exclude each other in the same patient.

A minor point of interest is that the patient discussed here is Negro. In the Enterline and Schoenberg article, it is stated that in reviewing all the previous literature, it is found that the race of the patient is not noted in 50 per cent of the cases reported, and that no Negro was reported in the other 50 per cent where mention is made of the race.

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Abnormal Electrocardiographic Findings in Spontaneous Pneumothorax

JAMES ROGERS FOX, M.D., F.C.C.P.
Minneapolis, Minnesota

It is common knowledge that the onset of spontaneous pneumothorax can simulate coronary occlusion, in fact this experience occurs quite frequently. Usually the differential is made by adequate history and inspection being substantiated by x-ray film. Once the diagnosis is established, an electrocardiogram is not thought of as significant in view of the pulmonary involvement. Apparently this is the reason for a recent unsuccessful perusal of the literature (both periodical and text) for data regarding electrocardiographic changes in spontaneous pneumothorax. This was prompted by a most interesting circumstance earlier this year. On the morning of April 12, the patient involved was given a complete physical examination on a routine basis. This included a chest x-ray film, but because of his age (21 years), an electrocardiogram was not included. The blood pressure was 120/82 and the heart and lungs were normal, although the rate was 88. The total physical status, including the chest x-ray film and laboratory work, was normal. The next morning (April 13) he arose with severe substernal pain and dyspnea. There had been no change in his routine. He reported immediately where upon one of the physicians ordered both an electrocardiogram and a chest x-ray film. He was perspiring profusely and had the appearance of collapse. The pain radiated to the left chest and side, the heart rate was 160; blood pressure 100/70; and temperature 98.2° F. He was hospitalized immediately. The direct writing electrocardiograph (Figure 1) showed tendency to right axis deviation, a rate of 100-110, a P-R interval of .26, very low T_1 and T_2 waves, U waves, and low R waves in the chest leads. A second electrocardiographer's report was "abnormal tracing—first stage heart block." The chest x-ray film then was seen to reveal pneumothorax of 90 per cent collapse on the left with the mediastinum shifted slightly to the right. There was also a minimal amount of fluid. When he was hospitalized, his blood pressure rose to 130/80, the respirations were 24, rate 108. He was given conservative management, including sedation and bed rest, and was discharged from the hospital after eight uneventful days. Thirteen days after the onset he was again x-rayed and an electrocardiogram was taken. At this time the left lung was completely expanded and the mediastinum was in position. The only residual was pleural thickening and adhesions noted on the left. The tuberculin test was negative. The electrocardiograph (Figure 2) had changed to show a vertical heart, but no axis deviation. The rate was 60-65 and the P-R interval—.16; the U waves were gone; the T waves more upright; and the chest lead R waves were greater. The tracing had reverted to normal. Unfortunately there had been no preceding base line tracing, which fact

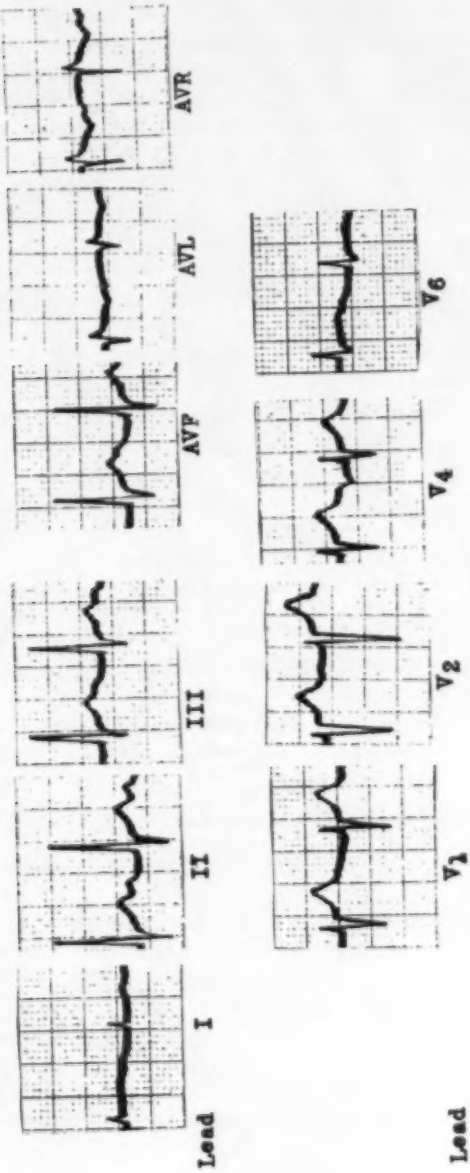

FIGURE 1

further indicates the desirability of doing an early single tracing, if possible, in all patients. Moreover, the presence of an earlier negative tuberculin test aided in light of the effusion.

Because of this experience and because of the lack of data in the literature, electrocardiograms have been taken at the onset of symptoms in five subsequent patients seen with spontaneous pneumothorax. In two the collapse was about 10-20 per cent; in two it was 25-40 per cent; and in one about 70 per cent. All but one of these (a 20 per cent collapse) were on the right and the mediastinum showed no shift by x-ray film in any of them. The P-R interval in the 70 per cent collapse showed only a variation which fell within normal limits. All the electrocardiograms were normal.

I should like to encourage the reporting of the electrocardiographic changes noted in spontaneous pneumothorax. We all expect the axis changes of mediastinal shift, But it would be well to document the others and note if there is a relationship to the per cent of collapse (as suggested in this group), the side involved, and the age of the patient. It will prove interesting to follow any future tracing changes in years to come.

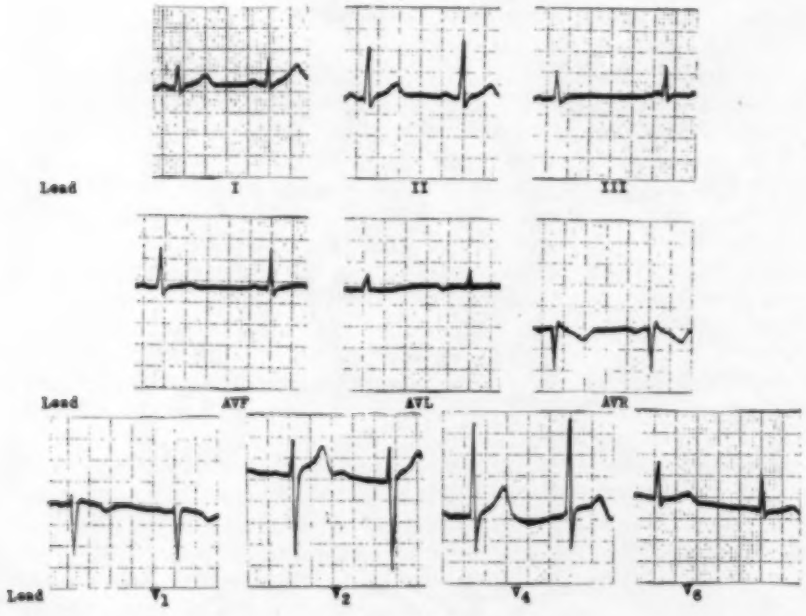

FIGURE 2

Teaching the Patient About His Chronic Pulmonary Diseases*

ROGER S. MITCHELL, M.D., F.C.C.P.**
Denver, Colorado

When an individual is stricken with an acute illness such as appendicitis, he usually need only accept the diagnosis, give his permission for operation, take the anaesthetic and tolerate the surgical after-effects for a short time. This treatment is administered almost entirely without his conscious participation.

When a patient becomes ill with a chronic disease, on the other hand, it becomes essential that he participate consciously and wholeheartedly in his treatment, and for many months as well. The fact that treatment of chronic lung disease usually necessitates both active and passive participation makes it mandatory that he be educated about his disease. Education becomes all the more important when the disease is contagious, as with pulmonary tuberculosis.

The education of the patient with chronic pulmonary disease is a cooperative project, involving the doctor, the nurse, the social worker and, most important, the fellow patient.

The development of rapport between the staff and the patient is unquestionably the first objective and is of the utmost importance. It begins the day each staff member first meets the patient; it is a continuing project; it is undertaken in widely varying ways, depending largely on the personalities involved. While it is gratifying to be regarded as a good fellow by your patients, this approach can be overdone. On the other hand, there is the opposite tendency of some professional personnel who strive to achieve strict and prompt obedience. Strict discipline will help establish a neat and and outwardly efficient hospital or clinic but not always a happy and successful one.

The subjects which should be stressed in such a patient education program are:

1. The mode of transmission of the disease (if infectious), and its prevention. For instance, we should encourage each patient to remind his fellow patient when he forgets to cover his mouth properly.

2. The anticipated future behaviour of the disease in the individual. Most patients appreciate a clear exposition of their problem and an estimation of their anticipated response to treatment. While harm can be done from excessive discussion of details, more harm is apt to be done by withholding pertinent information in the majority.

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*The twelfth in a new series of articles prepared under the sponsorship of the Council on Undergraduate Education of the American College of Chest Physicians.

**From the Colorado Foundation for Research in Tuberculosis and the University of Colorado School of Medicine.

3. The desire to get well. Motivation is a tricky subject, difficult to evaluate and even more difficult to arouse. Patient education can play an important part in stimulating motivation especially when the patient is unduly pessimistic about his prospects.

4. The prevention and control of fear of deformity, disability and death, which are thought to accompany thoracic surgery. A concise description of the operation to be performed will help. Arranging a chat with others who have had a similar operation may be invaluable.

5. The occasional unpleasantness of treatment. The treatment may be worse than the symptoms of the disease itself, especially after the first few weeks or months when symptoms may have abated. I have reference particularly to postural drainage, pneumoperitoneum refills, surgical operations, injections of various kinds and the taking of drugs (e.g. PAS) which may upset the stomach or cause other unpleasant symptoms.

The *sequence* of the problems as they are apt to present is as follows:

a. At *Diagnosis*. Here one must stress that the disease can be cured or controlled when there is good reason to believe this to be true. Of course, this optimistic point of view can be oversold in certain patients. One must also persuade the patient to accept treatment, which often seems far more drastic than appears justified by his feeling of ill health.

b. At entrance to the *Hospital*. Here he must be taught to accept a state of dependency for a time, that is, he must learn self-discipline. When certain drugs are begun for instance, the patient must be strongly admonished to avoid interruptions in their administration, except when approved by competent authority for good cause. This is also the point at which the patient must be persuaded to make sacrifices of time, comfort, convenience, even appearance if necessary, in order to get well.

c. *Surgical* Intervention. It is wise for the physician to start early, often months in advance, in preparing the patient to accept surgical intervention where this appears a probable eventuality. If circumstances change and no operation is required, no harm will have been done. In fact, most patients are pleased at such a favorable turn of events which can be laid to their credit. It is best to explain all procedures carefully to the patient; he often understands more than he is given credit for, even individuals without much of an education.

d. At *Discharge* from Hospital: Some patients do not want to be discharged, even though physically ready for this step. They have become so dependent that they do not wish to leave the comfort and security of the hospital and its staff. Some in this group were unhappy in their work or marital relations before becoming ill and are subconsciously unwilling to face these situations again. They can think of no alternative than to become reinvolved and unhappy once they leave; it is manifestly easier not to leave. Conscious and subconscious stratagems will be devised to avoid this threat. A comprehensive knowledge of the patient's personal and social history and an understanding of his personality plus great patience and tact may enable the physician to deal effectively with this common and trying situation.

The *methods* of patient education consist in movies, film strips, lectures, group discussions, pamphlets and bedside consultations by various professional personnel. It is important to remember that a point may be put across by the printed word, or better still, in a group session, which may have been difficult if not impossible to transmit by other means. One may also succeed in this regard by speaking to one patient within another patient's hearing, for the particular benefit of the latter.

Here are some *do's* and *don't's* worth remembering:

1. Don't rely upon one method of teaching.

2. Don't rely upon one teacher. This is a cooperative job.

3. Do check up on the effectiveness of pamphlets and other visual aids. Ask the patients whether they have understood what they have read and what they have been told when they are interviewed individually.

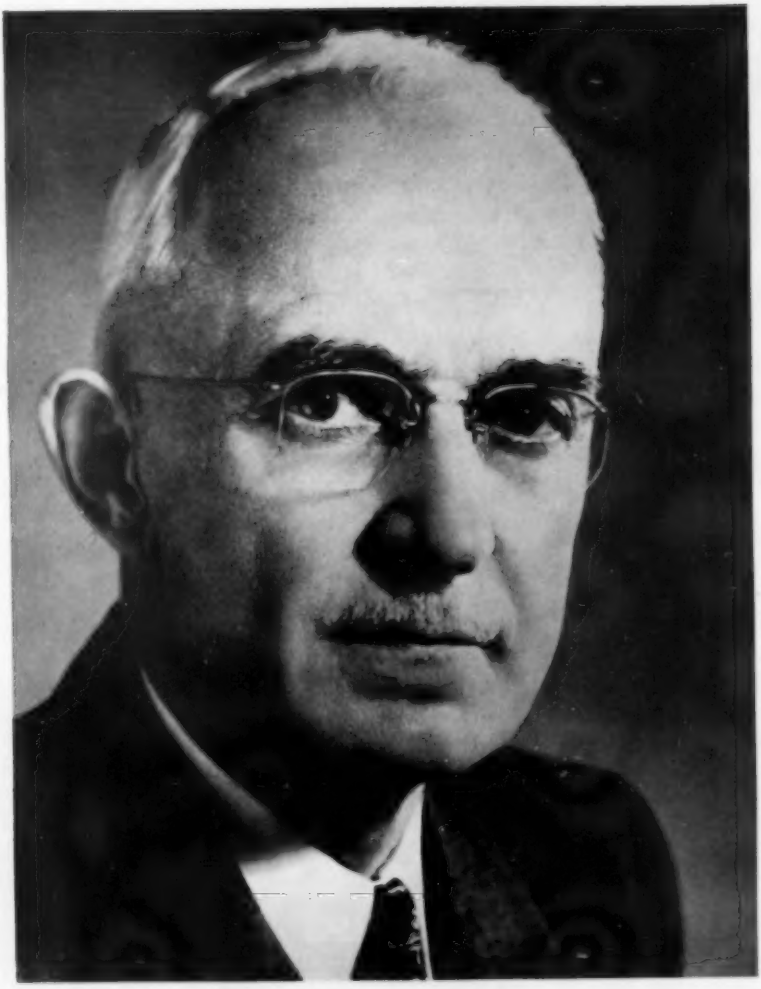
4. Do use simple non-scientific language.

5. Don't delay in starting patient education. It should begin immediately the diagnosis of chronic pulmonary disease has been made.

6. Do be *truthful* in informing patients or in answering their questions. This does not mean we should not avoid covering certain aspects of a problem which are better left untouched.

7. Don't leave the educational process to the hospital staff alone. The physician at home can do a great deal to augment the patient's knowledge about his disease and what he must do to protect others and to get well. On the other hand, the home physician may make use of the hospital as a "school" for his patients, especially for a few weeks or months at the outset of treatment.

In *summary*, teaching the patient about his chronic pulmonary disease is vitally important in its management. A good system to follow is first, to gain rapport with the patient, then pass out printed material; this should be followed by individual discussions at the bedside with the nurse, social worker and doctor. Then there should be group discussions including a question and answer period; this should be followed in turn by other bedside discussions. As the patient becomes ambulant, private discussions may be continued in the doctor's or social worker's office. From experience, it is clear that such a program is quite apt to fail in its objective unless there is considerable interest and enthusiasm on the part of the physician, no matter how interested the other personnel may be.



Henry Claris Sweany, M.D.

PRESENTATION OF THE COLLEGE MEDAL FOR 1956 TO DR. HENRY C. SWEANY*

Mr. President, Fellows of the College and Friends:

The great actor, John Barrymore, once said that the greatest disappointment in his life was that he had been denied the supreme pleasure of sitting in the audience to see himself act. Audience, I approach you this evening with a much more humble attitude.

In selecting the man for the college medal, the committee felt that he should be the full physician—teacher, author, researcher, administrator, clinician and humanitarian.

Henry Sweany was born in Cottage Grove, Oregon, August 1, 1890. He received his medical education at Northwestern University and Rush Medical College of Chicago. In the middle of his medical training, he found it necessary to go to work to finance his way through school. During this seven year interim he served as bacteriologist, sanitary chemist and assistant laboratory director of the Chicago Board of Health. After graduation in 1921, he was appointed Director of Laboratories and Research at the City of Chicago Municipal Tuberculosis Sanitarium where he remained for twenty-nine years. In 1950, he was appointed Chief Medical Director, Florida Tuberculosis Board, during the organization, building and staffing of three new hospitals, as well as establishing a treatment and research program. In 1955, he was appointed Director of Research, Pathology and Allied Sciences of the Missouri State Sanatorium, Mt. Vernon, Missouri.

The high point in his experience was at the Chicago Municipal Tuberculosis Sanitarium where he went to work to serve a few months but remained for over twenty-nine years. The need in the field was so great and the opportunity so compelling that he decided to remain and try to roll back the fog of ignorance that existed in tuberculosis at that time. During this period he contributed a great deal to the better understanding of clinical pathology in tuberculosis and other chest diseases.

During his varied medical career, about two hundred papers and monographs were published, many with one or more co-authors. They involved generally the pathology and bacteriology of chest diseases. It was because of his work at the Municipal Tuberculosis Sanitarium that several new procedures were inaugurated. He was the first in America to use the following: Cultures on a large scale in the routine diagnosis of tuberculosis; culture media for finding bovine bacilli directly from diseased tissues; the x-ray defraction method of determining detrimental silica in tissues; matched controls in the experimental treatment of tuberculosis; and blood chemistry methods in the hospitals of Chicago. The first recognized school in tuberculosis hospitals for laboratory technicians was established by him.

Dr. Sweany's various appointments have included Associate Professor of Medicine, Northwestern University Medical School; Professional Lecturer at the University of Chicago; Chief Consultant in Tuberculosis at the Hines Veterans Administration Hospital; Chief Consultant for the Carnegie Illinois Steel Company of Chicago; Consultant for various other industrial houses and railroads in Chicago. The offices held in medical societies include President of the American Trudeau Society; Vice-President of the National Tuberculosis Association; Chairman of the Section on Pathology and Physiology of the American Medical Association; and delegate to many International and Latin-American Tuberculosis congresses. He is Diplomate of the American Boards of Internal Medicine and Pathology. Since 1949, he has been an associate editor of the Journal, *Diseases of the Chest.*

He has received honorary certificates of membership in many Latin-American Tuberculosis Societies. He was a recipient of the Dearholt Medal of the Missis-

*Presented at the Presidents' Banquet, 22nd Annual Meeting, American College of Chest Physicians, Chicago, Illinois, June 9, 1956.

sippi Valley Trudeau Society in 1949. It is most fitting that in this great city of Chicago which he loves and loves him, that here we accord him this honor.

It is with great pride and affection that on behalf of the committee and the American College of Chest Physicians I present to Henry C. Sweany the 1956 college medal.

Arnold S. Anderson, M.D., St. Petersburg, Florida
Chairman, Committee on Awards

FOURTH INTERNATIONAL CONGRESS DISEASES OF THE CHEST

The Fourth International Congress on Diseases of the Chest, sponsored by the American College of Chest Physicians, will be held in Cologne, Germany, August 19-23, 1956, under the patronage of the German Federal Government. Chancellor Konrad Adenauer is the Honorary President of the Congress.

The following physicians will discuss the main themes of the Congress, as listed below. In addition, more than one hundred papers on diseases of the chest, including all aspects of cardiovascular and pulmonary diseases, will be presented by leading authorities from sixty-six countries and territories throughout the world. The popular Fireside Conferences will be presented each evening during the Congress, from 5:00 to 7:00 p.m. It is anticipated that more than 2500 delegates will register for the Congress. The Congress will be opened on Sunday evening, August 19, with a brilliant Inaugural Session.

Monday, August 20

Coronary Diseases: Claude S. Beck, USA; Houck E. Bolton, USA; W. Giese, Germany; Ralph Gregg, USA; M. Holzmann, Switzerland; Noboru Kimura, Japan; Jeremiah Stamler, USA; Ernst Wollheim, Germany.

Industrial Diseases of the Chest: E. W. Baader, Germany; Andrew L. Banyai, USA; L. Dautrebande, Belgium; R. H. Goetz, South Africa; G. S. Kilpatrick, England; Lopo de Carvalho, Portugal; Toussaint Turiaf, France; H. Valentin, Germany.

Tuesday, August 21

Chemotherapy in Tuberculosis: Etienne Bernard, France; Gerhard Domagk, Germany; Ludwig Heilmeyer, Germany; J. Hirsch, Switzerland; Gertrude Meissner, Germany; J. Arthur Myers, USA; A. Omodei Zorini, Italy; Hans Rink, Germany; Hans Wurm, Germany.

Wednesday, August 22

Pulmonary Function: S. Bjorkman, Sweden; Wilhelm Bolt, Germany; Charles Fletcher, England; C. W. Hertz, Germany; P. Sadoul, France; Raul Vaccarezza, Argentina; W. G. Zijlstra, Holland.

Cardiac Function: A. de la Fuente Chaos, Spain; Ovidio Garcia-Rosell, Peru; Burgess L. Gordon, USA; Josef Jacobi, Germany; W. Knipping, Germany; H. Reindell, Germany; K. Wexler, Germany.

Thursday, August 23

Tumors of the Mediastinum: Maurice J. Bariety, France; Anthony Caralps, Spain; H. Krauss, Germany; M. Loeweneck, Germany; Richard H. Overholt, USA; E. Uehlinger, Switzerland; H. Venrath, Germany.

Panel discussions will follow each of the above sessions. The names of the panelists will appear in the final program. The official languages are German, French, Spanish and English; there will be simultaneous translation of the discussions into the official languages.

Officers: President, Gerhard Domagk; Vice-President, Hugo W. Knipping; General Secretary, Josef Jacobi; Chairman, Executive Committee. Joachim Hein; Executive Committee: Otto Buurman; Ernst Schwering; Max Adenauer; Ludwig Heilmeyer; Rudolph Schoen; Walter Unverricht; Ernst Wollheim; Hans Wurm; and Rudolf Zenker; Andrew L. Banyai, Chairman, Council on International Affairs; Murray Kornfeld, Executive Director.

ANNUAL MEETING AND ELECTION OF OFFICERS

The 22nd Annual Meeting of the American College of Chest Physicians was held at the Hotel Sherman, Chicago, Illinois, June 6 through 10. More than 1,400 members and guests registered for the meeting which included 1,100 physicians. Thirty-two technical exhibits were displayed throughout the meeting.

Fellowship certificates were awarded to 250 physicians at the Annual Convocation of the College held on Saturday, June 9, and more than 600 physicians and their families attended the President's Banquet which followed.

In a special ceremony during the Convocation, the Cuban Chapter presented their national flag to the College for permanent display at the Executive Offices. Since this first presentation many chapters throughout the world have expressed a desire to present their country's flag to the College. Arrangements are being made for their presentation during the International Congress in Cologne, Germany, August 19-23, 1956.

The following Officers, Regents, and Governors were elected:

OFFICERS

President:	Herman J. Moersch, Rochester, Minnesota
President-Elect:	Burgess L. Gordon, Philadelphia, Pennsylvania
1st Vice-President:	Donald R. McKay, Buffalo, New York
2nd Vice-President:	Seymour M. Farber, San Francisco, California
Treasurer:	Charles K. Petter, Waukegan, Illinois
Assistant Treasurer:	Albert H. Andrews, Chicago, Illinois
Chairman, Board of Regents:	John F. Briggs, St. Paul, Minnesota

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District 1:	Edward A. Greco, Portland, Maine
District 5:	M. Jay Flipse, Miami, Florida
District 8:	Alfred Goldman, St. Louis, Missouri
District 13:	Harold G. Trimble, Oakland, California
District 15:	Jaime F. Pou, Hato Rey, Puerto Rico
District 16:	Hastings D. Walker, Honolulu, Hawaii
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Arizona:	Howell S. Randolph, Phoenix
Arkansas:	William P. Gray, Batesville
Colorado:	W. Bernard Yegge, Denver
District of Columbia:	Edgar W. Davis, Washington
Florida:	Arnold S. Anderson, St. Petersburg
Idaho:	Kenneth A. Tyler, Gooding
Kansas:	Charles F. Pokorny, Halstead
Maine:	George E. Young, Skowhegan
Maryland:	Otto C. Brantigan, Baltimore
North Carolina:	Ralph E. Moyer, Oteen
North Dakota:	Paul J. Breslich, Minot
Pennsylvania:	Ross K. Childerhose, Harrisburg
Texas:	George R. Herrmann, Galveston
Virginia:	Everett C. Drash, Charlottesville
Washington:	Norman Arcese, Seattle
West Virginia:	George R. Maxwell, Morgantown
Manitoba (Canada):	Lawrence R. Coke, Winnipeg

The 23rd Annual Meeting of the College will be held at the Hotel Commodore, New York City, May 29-June 2, 1957. The American Medical Association will hold its annual meeting in New York City, June 3 through 7, 1957.

College Chapter News

VENEZUELA CHAPTER

Under the chairmanship of Dr. Jose I. Baldo, Regent of the College for Venezuela, the Venezuelan Chapter held a special meeting at the National Institute of Tuberculosis in Caracas on April 21. It was decided that the annual meeting of the chapter would be held in Merida on December 9, at the time of the III International Congress on Phthisiology which will take place December 8-11.

Seated, left to right: Drs. A. Gabaldón Parra; Carlos Ortega G.; Juvenal Curiel; Julio Criollo Rivas (Governor, Central-Eastern Zone); José Ignacio Baldó (Regent and Chairman, Council on Pan American Affairs); Pedro Iturbe (Governor, Western Zone); Rogelio Valladares G. (Secretary-Treasurer), and Rubén Jonckheer. *Second row*: Drs. Luis Lozano Gómez, Alejandro Príncipe, Rafael Gallardo, Julio Rodríguez, Ladislao Pollak, Juan Delgado Blanco, Victor Giménez and Jorge Echeverría C. *Third row*: Drs. José M. Mejía Carrillo, Luis Gómez López, Humberto Delgado Rivas, Carlos Zubillaga, Ramón Soto Matos, Galdino Tattoni, José H. Valero Lugo and Victor Yéspica.

BARCELONA (SPAIN) CHAPTER

A panel on tuberculosis was presented by the Barcelona Chapter at the Instituto Antituberculoso on April 14, in which the following members of the chapter participated: Drs. M. Gonzalez Ribas, J. Oriol Anguera, A. Castella Escabros, T. Seix Miralta, J. Civil Ingles, E. Bieto Reiman, and J. Bolas Almenar.

JAPANESE CHAPTER

A special meeting of the Japanese Chapter was held on May 14 at the Kitazato Memorial Hall, Keio University School of Medicine, Tokyo, at which Dr. Roger H. L. Wilson, San Francisco, California, spoke. Dr. J. Garaix of Paris, France was also a guest speaker. The following scientific program was presented:

"Clinico-physiological Aspect of Intrapulmonary Gas Distribution"
H. Sasamoto, Tokyo

"Influences of Pneumoperitoneum Upon Various Organs"
N. Wada, Tokyo

"The Elevation of Bronchoscopic Diagnosis in Lung Cancer"
J. Garaix, Paris, France

"Principles of Nutrition in the Treatment of Tuberculosis"
Nancy L. Wilson, B.S., San Francisco, California

"Clinical Physiology in Chest Disease"
Roger H. L. Wilson, San Francisco, California

The scientific session, which was attended by more than 100 physicians, was followed by a dinner given in honor of Dr. and Mrs. Wilson at the International House.

Members of the Japanese Chapter at a special meeting held in Tokyo, May 14 honoring Dr. and Mrs. Roger H. L. Wilson.

NEW CHAPTER OFFICERS

LOUISIANA CHAPTER

President:	Lawrence H. Strug, New Orleans
President-Elect:	Frank A. Pickell, Baton Rouge
Secretary-Treasurer:	Howard Buechner, New Orleans

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President:	Ida Levine, Brooklyn
1st Vice-President:	Francis W. O'Donnell, Buffalo
2nd Vice-President:	Emil Naclerio, New York
Secretary-Treasurer:	Harry Golembe, Liberty (re-elected)

URUGUAY CHAPTER

President:	Juan Soto Blanco, Montevideo
Secretary-Treasurer:	Rene Racine, Montevideo

BOOK REVIEW

THERAPY OF FUNGUS DISEASES: AN INTERNATIONAL SYMPOSIUM. Edited by Thomas H. Sternberg, M.D., Professor of Medicine (Dermatology) and Assistant Dean for Postgraduate Medical Education, and Victor D. Newcomer, M.D., Associate Professor of Medicine (Dermatology). Little, Brown and Company, Boston and Toronto, 1955.

The current need for a work bringing together up-to-date information by outstanding researchers in the field of mycotic diseases has at last been fulfilled. The symposium reported in this book was planned to stimulate an exchange of ideas on a national and international level dealing with the therapy of fungus infections.

Eighty-four contributors, dealing with all phases of fungus diseases, have combined their efforts to bring to us the results of their latest research. Although the newer therapeutic agents are discussed in complete scientific detail certain fundamental aspects such as the soil as a natural reservoir for human pathogenic fungi, the ecology and spread of pathogenic fungi, an evaluation of the laboratory methods for listing fungicides, the influence of hormonal conditions on experimental fungus infections, pathogenesis and immunology, and the problem of active immunization, have been covered.

Among the newer therapeutic agents discussed are the aromatic diamidines, cinnamic acids and the nitrostyrenes, filipin, the various sulfonamides and sulfur compounds, chlorquinaldol, neomycin, NEPERA (1968), nystatin, actidione, aminostilbamidine, MRD-112, stilbamidine, 2-hydroxystilbamidine, rhodanine and related compounds, and antihistaminics.

It was stressed there are no practical methods of immunization and that in only two of the deep fungus infections, blastomycosis and sporotrichosis, are the methods of treatment reasonably satisfactory.

It is my opinion this book, edited by Drs. Sternberg and Newcomer, would be an invaluable addition to the library of clinicians interested in this important field of medicine.

Alvis E. Greer, M.D.

CALENDAR OF EVENTS

NATIONAL AND INTERNATIONAL MEETINGS

Fourth International Congress on Diseases of the Chest
Council on International Affairs
American College of Chest Physicians
Cologne, Germany, August 19-23, 1956

Interim Session, American College of Chest Physicians
Seattle, Washington, November 25-26, 1956

POSTGRADUATE COURSES

11th Annual Postgraduate Course on Diseases of the Chest
Hotel Knickerbocker, Chicago, October 15-19, 1956

9th Annual Postgraduate Course on Diseases of the Chest
Park-Sheraton Hotel, New York City, November 12-16, 1956

CHAPTER MEETINGS

Colorado Chapter, Estes Park, September 3, 1956

Kentucky Chapter, September 18-20, 1956

Michigan Chapter, Detroit, September 27, 1956

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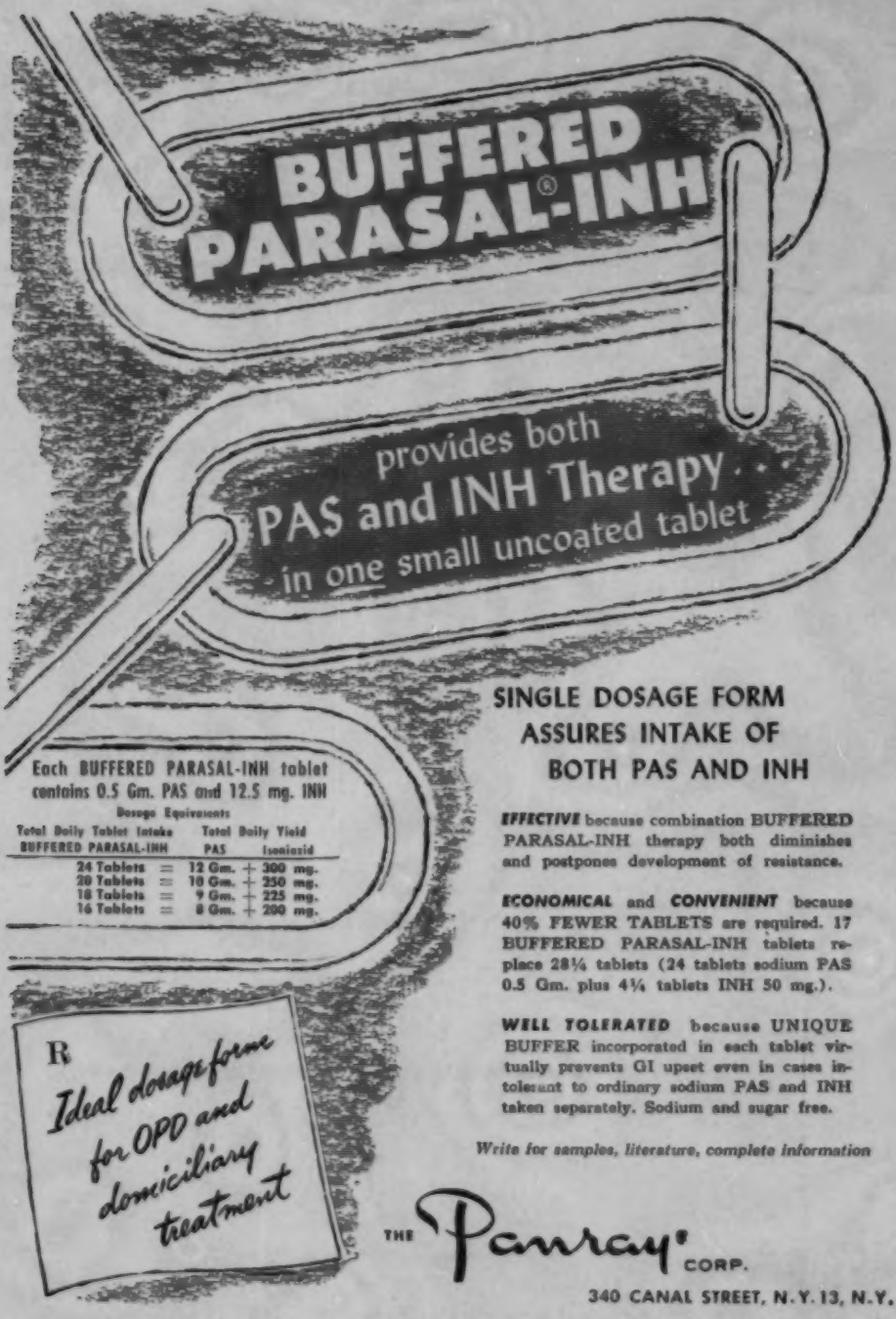

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